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Psychosomatic aspects of endometriosis-associated pain

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zur Erlangung der Doktorwürde der Medizinischen Fakultät
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Contents

1. Abstract

Background: Chronic pelvic pain (hereafter CPP), and severe dysmenorrhea are the most common symptoms of endometriosis. Despite CPP being common amongst women with endometriosis, the underlying pathophysiological mechanisms of endometriosis-associated pain have not been fully understood. Some previous studies reported correlations between the genesis of endometriosis and psychosomatic factors including personality, mood disturbance and childhood events, while some other researchers have attempted to identify a psychopathological causation of CPP. The current study aims to systematically investigate these links, and to focus in particular on their role in the development, perception and regulation of endometriosis-associated pain.

Methods: We examined the most common psychological factors that have been linked with the intensity and aggravation of CPP, and the development of endometriosis. Additionally, we investigated the following three characteristics of endometriosis that can affect the appearance of pain: stage, location of the endometrial lesions, and the presence/type of adhesions. We distributed questionnaires addressing the quality of life and other personal characteristics to various Swiss hospitals and self-help organizations in Germany. The control group consisted of women without endometriosis, some of whom were afflicted with chronic pain due to an illness other than endometriosis. The endometriosis group diagnosis was confirmed through laparoscopic and histological examinations. 208 people were included in this study: 104 endometriosis patients, and 104 belonging to the control group.

Results: Endometriosis patients, who suffer from chronic pain, had a higher prevalence of depression as well as psychiatric problems. The prevalence of physical and emotional abuse, both in childhood and in adult life, was higher among endometriosis patients with CPP than among pain-free women. Additionally, a difficult acceptance of a patient's menarche and of the physical changes through adolescence was linked with pain aggravation. The majority of our endometriosis patients were in endometriosis stage IV. We found neither a significant correlation between the stage of endometriosis and the intensity of pain, nor between the pain's daily duration and frequency. We confirmed that there is a positive correlation between pain intensity and the existence of adhesions, although we found no link between pain intensity and the location of the adhesions.

Conclusions: Our investigation shows that endometriosis patients who suffer from chronic pain had a higher prevalence of depression as well as anxiety. We found that people with

specific personality characteristics as a neurotic personality and mental disorder seem to develop chronic pain and disability more often. A higher prevalence of physical and emotional abuse, both in childhood and in adult life was correlated with the presence and experience of pain. Causes of pain in endometriosis are multifactorial. Personality characteristics and childhood events are strongly associated in the appearance and regulation of pain.

2. Introduction

Endometriosis, the development of endometrial tissues outside the lining of the uterus, is one of the most common benign gynecological conditions. It affects 7 - 10% of the female population, with 75% of all patients being of reproductive age [1, 2, 3]. The reported recurrence rate of the disease is high, estimated as 21.5% at 2 years and 40–50% at 5 years [4].

Causes: Regarding the origin of endometriosis, many causes are discussed. The precise pathogenesis is not clearly established but one of the most widely accepted hypothesis involves retrograde menstruation and the reflux of endometrial tissue implants, through a hyperperistaltic-dystocic uterus, on the surface of the ovaries and peritoneum [5]. Although retrograde menstruation occurs to some degree in all women, only those who are unable to clear the menstrual debris because of immune dysfunction will go on to develop endometriosis [6]. Evidence also supports that the lymphatic or circulatory system can also transport endometrial cells to distant sites [7]. Findings of endometriosis in unusual locations support this theory. Additionally, the theory of coelomic metaplasia suggests that the parietal peritoneum can undergo metaplastic transformation to tissue histologically indistinguishable from the normal endometrium [7]. This theory is attractive in cases of endometriosis in the absence of menstruation such as in premenarchal and postmenopausal women.

Diagnosis: The diagnosis of pelvic endometriosis cannot be made with absolute certainty without a laparoscopy [8]. During the procedure, detailed notes of the extent, type and sites of the lesions must been taken, as well as histological biopsies in order to stage the disease between the I–IV stages according to the Revised Classification of the American Society of Reproductive Medicine, ASRM, Table 1, [9]. However, as diagnostic laparoscopy and excisional biopsy are invasive procedures with distinct morbidity and mortality, medical health care providers often hesitate to decide in favor of surgery. This hesitation also attributes to the diagnostic delay of endometriosis. The average time between first symptoms and diagnosis of endometriosis is between 6 to 11 years [10]. The diversity and lack of specificity of the symptoms can also attribute to this diagnostic delay [11].

Endometriosis includes a broad spectrum of symptoms, from accidental diagnosis to a chronic disabling disease [12]. Chronic pelvic pain (CPP) and severe dysmenorrhea are the most common symptoms of endometriosis [8]. However, there are patients in the aggravated endometriosis stage that have never experienced any symptoms during their illness.

Symptoms other than CPP and severe dysmenorrhea include dyspareunia, infertility, menstrual irregularities, cyclical hematuria, rectal bleeding as well as painful defecation, exhaustion and fatigue [8].

The dominant feature that mostly influences patients' life is the experience of CPP that is observed in approximately 30% - 50% of patients [8, 13]. CPP is defined as pain in the area of the pelvis that has been present for more than 6 months [13]. In many cases the pain itself is the symptom that leads to the diagnosis of the disease. It is usually described as severe, wave-like, with periods of no pain, along with peaks of intense pain, especially near menstruation [13]. It is one of the most common gynecological complaints, estimated to comprise 2-10% of outpatient gynecological referrals [2]. Endometriosis is responsible for almost 12% of these referrals [2].

The mechanism by which endometriosis causes pain and very often hyperalgesia is poorly understood. Most probably the causes and the perception of pain in endometriosis are multifactorial, determined by a complex system of somatic and psychosomatic factors.

From a somatic point of view cyclical bleedings within the endometriotic lesions, which generally contain clusters of hemorrhages and hemosiderin-laden macrophages, can be responsible for hyper-pressure and pain [14]. It has also been demonstrated that endometriosis itself can produce and release prostaglandins, inflammatory mediators such as kinin, histamine, interleukin that can stimulate sensory nerve endings [15, 16]. Furthermore, nerve growth factor (NGF), which plays a key role in the occurrence of pain, hyperalgesia, and neuropathic pain, is strongly expressed in deep infiltrating endometriosis, and its specific receptor (Trk-A) is expressed in nerves lying within deep lesions or in the vicinity of deep endometriotic lesions [14].

At the same time, the absence of a correlation between the extent of endometriosis and the intensity, and even the presence of pain, suggests a possible link between the personality of the affected women and the perception of pain [11]. The complex interactions between psychological strain and pain indicate that endometriosis-associated pain is strongly affected by psychosomatic factors. The permanently increased stress level in chronic pain patients, depression and sleep disorders that are more prevalent among women with CPP may influence pain reactions [17]. Persistent pain is often associated with despair, resignation, hopelessness and depression, which may form a vicious cycle [11]. Living with chronic pain in endometriosis patients remains an untreatable symptom in most cases. This leads to frustration, fear and anxiety for their future. This pessimistic attitude regarding their pain

control can be associated with a reduced pain response and may aggravate symptoms [11].

Therapy: Current therapies for the management of endometriosis and endometriosis-related symptoms are medical, surgical, or both. Medical therapies intend to induce a hypoestrogenic state to reduce menstrual flow and increase the apoptosis of endometriotic lesions [10]. They include androgenic or progestational compounds and gonadotropin-releasing hormone analogs, which are comparably effective [10]. Although surgery to remove endometriosis is effective in relieving pain and restoring fertility, in some cases recurrence of symptoms is common, and repeated medical and surgical interventions are often needed [18, 19]. About 20% of women show recurrent disease symptoms, especially pelvic pain, within 12 months after treatment [11].

The failure to treat endometriosis successfully in the long term underscores the pressing need for the development of a more efficacious strategy for treating endometriosis. Medical support until now has concentrated on somatic therapies, targeting only the organic causes of the disease and endometriosis' symptoms. The important role that a chronic painful disease has on quality of life and the experience of pain has until now been neglected. Only recently medical support has begun to consider the role of different psychological and social characteristics of the affected population as co-factors in the pathogenesis and the perception of pain. In particular, the investigation of psychosomatic aspects in endometriosis-related pain and pain management is a very young field of research. Some studies tend to focus on the search for psychiatric abnormalities and significant incidences of childhood and family dysfunction in women with CPP [20, 21, 22]. However, the relationship between psychological factors and chronic pain is not understood and the results of the existing, limited-in-number, studies have been contradictory [23, 24].

The aim of the present study was to investigate the characteristics of endometriosis-related pain by focusing on the psychosocial and psychosomatic characteristics of the patients and their potential roles in the development and perception of pain. Psychiatric morbidity, personal characteristics, and significant childhood events, (that in the past have been linked with patients with CPP), was examined among endometriosis patients and the healthy population. Two comparisons were made: The first between endometriosis patients and women without endometriosis. The second was made between chronic pain patients with and without endometriosis. It was hoped that the investigation of the link between different psychiatric and psychosocial factors and the experience of pain will lead us to conclusions that point out the importance of various psychosomatic factors in the genesis, experience and progression of endometriosis-associated chronic pain. Accordingly, this would aid in the

recommendation of treatments, in which the psychosomatic aspects of the disease can be integrated into medical care.

3. Motivation

Chronic pelvic pain in endometriosis patients is a common symptom. Despite the variety of surgical and pharmacological treatment options, it remains a burden to the sufferers. The early identification of certain psychological patterns among chronic pain endometriosis patients will be beneficial in providing alternatives for pain management. A departure from a pure somatic approach to a psychological one will provide physicians and patients with all-rounded treatment options.

To facilitate this approach, the psychological factors influencing chronic pain in endometriosis patients need to be investigated. These factors primarily include depression, personality characteristics and negative childhood experiences. This project was designed to compare and correlate these psychological variables. We are contributing to the scarce literature on psychological aspects among endometriosis patients with chronic pain. The few studies done in this area previously have been found lacking in methodological approaches – often due to small sample sizes, using multiple pain populations, and a failure to make distinctions between causes and effects [25, 26, 27].

Work has been carried out investigating the influences of these psychological factors on general (not endometriosis related) chronic pain. Also, literature on the influence of a variety of psychological factors on the development of endometriosis has been done. Both research efforts have, for example, depression, childhood abuse, and personality characteristics as investigated variables in common. We are at a position in which we can successfully combine these two fields of research: we use the psychological factors typically examined for the development of endometriosis, except applied not to disease development itself, but rather to the progression, perception, and regulation of chronic pelvic pain in endometriosis patients.

4. Materials and Methods

4.1 Study design

The present study was approved by the Swiss Ethics Commission and was part of an ongoing study started in January 2008.

The study was designed as a cohort study, comparing data from women with endometriosis to those of women without endometriosis (control group). Main outcome measures were the intensity and duration of the pain. Secondary outcome measures included the association between the stage of endometriosis according to the Revised American Society for Reproductive Medicine classification (ASRM), table 1 [9], the location of endometriosis lesions as well as the presence of deep infiltrating endometrial herds and CPP.

10	**Endometriosis**	< 1 cm	1-3 cm	> 3 cm
	Superficial	1	2	4
	Deep	2	4	6
Ovary	R Superficial	1	2	4
	Deep	4	16	20
Ovary	L Superficial	1	2	4
	Deep	4	16	20
	Posterior Cul-de-sac Obliteration	Partial 4		Complete 40
	Adhesions	< 1/3 Enclosure	1/3-2/3 Enclosure	> 2/3 Enclosure
Ovary	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16
Tube	R Filmy	1	2	4
	Dense	4[1]	8[1]	16
	L Filmy	1	2	4
	Dense	4[1]	8[1]	16

Tbl. 1: American Society for Reproductive Medicine revised classification of endometriosis.
Staging: Stage I (minimal): 1-5; stage II (mild): 6-15; stage III (moderate): 16-40; stage IV (severe): > 40.
R= right, L= left

4.2 Questionnaire

All study participants completed a self-administered questionnaire designed to investigate their psychological status and personality, their experience through childhood: in particular the presence of sexual and physical abuse during childhood. In addition the medical status, their partnership, sexual and professional life were examined. The questionnaire included validated questions to evaluate pain (Brief Pain Inventory = BPI), mood symptoms (Brief Symptom Inventory = BSI), anxiety (Perceived Stress Questionnaire = PSQ20, Patient Health Questionnaire = PHQ, Sense Of Coherence = SOC-9), childhood (modified form of Childhood Trauma Questionnaire = CTQ), partnership (Partnerschaftsfragebogen = PFB) and sexual life (from a modified form of Brief Index of Sexual Functioning and Global Sexual Functioning) as well as questions developed from the investigators based on current research to investigate study participants' experiences regarding their menarche and the maternal reaction to menarche.

Age, nationality, height and weight, monthly income, marital status, life style habits (diet, nutritional preferences, smoking, drug habits) and parity were noted. In order to investigate the participants' education levels, education was divided into 3 categories: the first category included participants with a technical college and a university degree and was characterized as "high education", while the "basic and low education" category included people with primary education and a high school diploma. The third category included participants that gave either no answer to this question or chose the answer "other" as a possible question. This category was characterized as "unclear". To investigate the influence of the Body Mass Index (BMI) on the pain, the participants were divided into 5 categories corresponding to their BMI = "underweight" with a BMI <19, "normal weight" for BMI=19-24, "overweight" for BMI=25-30, "adiposity" for BMI=31-40 and "strong adiposity" for BMI>40.

The participants with endometriosis were divided into four endometriosis groups according to the Revised American Society for Reproductive Medicine classification (ASRM), table 1. The ASRM score was obtained for each of the laparoscopy-positive patients.

The time between the presence of the first symptoms and the diagnosis of endometriosis, the stage of the disease at the time of the first diagnosis, the current stage of the disease and the number of surgical interventions prior to study period were noted. Different medical therapies

and their efficacy were examined (yes or no answers). Satisfaction with medical support was explored using a yes/no answer choice. The questionnaire also included a question on psychological support treatment (yes, no answer) and its efficacy on treating endometriosis. The patient had to put a mark between 0% (no efficacy) and 100% (complete efficacy).

All patients with pain were asked to record the duration, frequency and intensity of pain. The patients characterized their pain using the Visual Analog Scale (VAS), estimating their pain on a scale from 0 (indicating no pain) to 10 (the worst pain imaginable). Patients were asked to estimate the intensity of i) the most severe pain experienced over the last 24 hours, ii) the least severe pain the last 24 hours, iii) the average pain experienced in the last 4 weeks, iv) the pain experienced at the moment.

Using the Pain disability index (PDI) and the Brief Pain Inventory (BPI), patients with chronic pain were asked to evaluate the influence of their pain while performing various day-to-day activities like sleeping, eating, relationship with their children and partner, sexual and social activities. A scale from 0 to 10 was used to express their everyday disturbance. 0 indicated no disturbance and 10 the most severe disturbance.

The Pain disability Index (PDI) is a simple and rapid instrument for measuring the impact that pain has on the ability of a person to participate in essential life activities. 7 categories of life activity are included in the question set: 1. Family and home responsibilities: activities related to home and family, 2. Recreation: hobbies, sports and other leisure-time activities, 3. Social activity: participation with friends and acquaintances other than family members, 4. Occupation: activities partly or directly related to working including housework or volunteering, 5. Sexual behavior: frequency and quality of sex, 6. Self-care: personal maintenance and independent daily living (bathing, dressing etc.), 7. Life-support activity: basic life supporting behaviors (eating, sleeping etc.). By adding the numbers up, one can arrive at a score between 0 and 70. The higher the index, the greater the person’s disability due to pain [28].

The Brief Pain Inventory (BPI) is a short, self-administered and frequently used pain assessment tool that was initially developed for use in cancer patients. The BPI measures both the intensity of pain (sensory dimension) as well as the interference of pain in the patient's life (reactive dimension). It also

queries the patient about pain relief, pain quality, and patient perception of the cause of pain. Participants are asked to rate their pain intensity as its “worst”, “least”, “average” and “current” and to rate the extent to which pain interferes with 7 daily activities and enjoyment of life including general activity, walking, work, mood, enjoyment of life, relations with others, and sleep. A 0-10 numerical rating scale is used to measure pain severity where 0 = no pain and 10 = pain as bad as one can imagine. The interference items are measured using a five-option verbal description scale, with ratings 0 = not at all, 1 = a little, 2 = moderate, 3 = quite a lot, 4 = an extreme amount. Patients are also asked to provide their pain location(s) and to describe the perception of the cause of pain, the types of pain treatment they are receiving, and the amount of the relief providing by the treatment [28].

To investigate whether or not people with pain had more anxiety and more psychological stressors, we used validated questionnaires as mentioned before. These questionnaires are commonly used in clinical practice to recognize and diagnose depression and anxiety: the General Anxiety Disorder-7 questionnaire (GAD-7) and the Prime Health Questionnaire (PHQ-9) about Depression Severity [29, 30].

The GAD-7 (Generalized Anxiety Disorder Questionnaire) is a practical self-report anxiety questionnaire that can help catch an increase in anxiety before it becomes disabling. Using a response set of seven questions helps to diagnose generalized anxiety disorder. The following questions are included: 1. Feeling nervous, anxious, or on edge, 2. Not being able to sleep or control worrying, 3. Worrying too much about different things, 4. Trouble relaxing, 5. Being so restless that it is hard to sit still, 6. Becoming easily annoyed or irritable, 7. Feeling afraid, as if something awful might happen. Each question has a numerical value from 0 to 3. By adding the numbers up, one can arrive at a score between 0 and 21. A score of 10 or higher means that significant anxiety is present [29].

The PHQ-9 depression scale is a short-in-length depression measure, which along with the following nine factors, establishes depressive disorder diagnoses as well as grade depressive symptom severity: 1. Having little interest or pleasure in doing things, 2. Feeling down, depressed, or hopeless, 3. Having trouble falling or staying asleep, or sleeping too much, 4. Feeling tired or having little energy, 5. Having poor appetite or overeating, 6. Feeling bad about oneself - or that you are a failure or have let oneself or your family down, 7. Having trouble concentrating on things, such as reading the newspaper or watching television, 8.

Moving or speaking so slowly that other people could have noticed. Or the opposite - being so fidgety or restless that one has been moving around a lot more than usual, 9. Having thoughts that one would be better off dead or hurting yourself in some way. The PHQ-9 score ranges from 0 to 27, because each of the 9 items can be scored from 0 (“not at all”) to 3 (“nearly every day”). Easy-to-remember cutoff points of 5, 10, 15 and 20 represent the thresholds for mild, moderate, moderately severe and severe depression [30].

The questionnaire also canvassed the prevalence of various mental diseases such as panic attacks/stress, suicidal thoughts in the two groups with five predefined answers. Women were also asked whether they had ever been under psychiatric or psychological treatment as well as the reason for hospitalization, if it occurred.

Abuse against the mother, drug abuse in the family, the existence of a retarded family member, the experience of a family member committing suicide and imprisonment, were situations that were examined to characterize a problematic family during childhood.

Further questions explored physical (bruises, factures, hospitalization) and sexual abuse (verbal sexual abuse, touching, attempting or having intercourse) during childhood.

To investigate the perception of menstruation, women were asked to evaluate their memories of their first menstruation as well as the reaction of their mother to it. Further questions concentrated on the characteristics of menstruation (duration, dysmenorrhea), to ascertain whether or not the perception of menstruation was independent of the presence of dysmenorrhea and the menstruation duration.

Additional non-standard questions about socio-demographic characteristics, life-style, medical history, professional and career details, medical treatments, doctor-patient relationships, and validated questionnaires about partnership und sexuality (Global Sexual Functioning Questionnaire, Brief Index of Sexual functioning for Women) had to be answered by the study participants. For the purpose of this thesis, only the questions related to endometriosis-associated pain, psychological characteristics (depression, anxiety), experience of menstruation and childhood experiences were evaluated.

4. 3. Patient selection and recruitment

The questionnaires were distributed to two groups of women: Women with endometriosis (the patients) and women without endometriosis (the control group). The two groups had same demographic-social characteristics: All were women in their reproductive age (between 18-55 years old) who were mentally healthy and could speak fluent German. Pregnant women, or women with psychiatric diseases were excluded from our study. The age (+/-5 years), the nationality, the civil status and education status were used as matching criteria between the two groups. The parity status was excluded as matching criteria as women with endometriosis have high prevalence of infertility.

Recruitment of study participants was performed in cooperation with different hospitals in Switzerland and Germany. While the control group consisted of women without endometriosis, some of them were afflicted with chronic pain due to an illness other than endometriosis. Control women were recruited from women presenting for annual routine examination in different gynecological offices and hospitals, or of women who had been hospitalized for a reason other than endometriosis. Annual routine check-ups were chosen to reduce selection bias to social status, as nearly all women in Switzerland and in Germany undergo routine gynecological examinations. Table 2 presents the distribution of the control group.

The recruitment of the patient group was performed in cooperation with the self-help endometriosis group in Germany, Leipzig and various hospitals in Switzerland (see Table 3). The endometriosis support group in Leipzig, Germany, is a society that provides support, help, advice and information for women with endometriosis and their families. The Leipzig center conducts frequent meetings of the leaders of the self-help groups in which our project was presented, and questionnaires were distributed via the Leipzig center to different self-help groups. Our questionnaire was also available on the Leipzig center website so that interested women could participate – after their diagnosis was verified.

The endometriosis group was confirmed through laparoscopic and histological examinations, and included women who had been through at least one operation that had revealed a positive histology for endometriosis. Women with a histologically verified endometriosis diagnosis were included in the patient group, regardless of the time of diagnosis or operation date. The

patients were initially contacted either personally or telephonically in order to participate in our study. It was emphasized that participation was voluntary.

Each participant additionally received the project brief, and gave informed and signed consent to participate in our study. Additionally, the endometriosis group gave written consent, so that their diagnosis could be verified with medical charts. After providing information on the study, and obtaining the patient's consent, verification of inclusion/exclusion criteria, the questionnaire was distributed.

208 people were finally included in this study: 104 endometriosis patients and 104 belonging to the control group.

Women presenting for annual routine gynecological examinations (area Zurich, Switzerland) or women being hospitalized for a reason other than endometriosis in the university hospital of Zurich or in regional hospital of Luzern, Switzerland	79% (82)
Friends of women with endometriosis in the area of Germany, Leipzig	21% (22)
Total control group	**100% (104)**

Tbl. 2: Recruitment of the control group

Endometriosis patients from Germany, Leipzig (self-help group of endometriosis)	64% (67)
Patients from the gynecological department the university hospital in Zurich, Switzerland (USZ) and from Dr. Sillem, chief doctor of Emmendingen hospital, Germany	36% (37)
Total patients	**100% (104)**

Tbl. 3: Recruitment of the patients group

4. 4. Operation reports

The operation reports, accompanied with the histological results of the removed tissue to confirm the disease and the discharge reports from all endometriosis patients were collected. After being classified according to the rASRM criteria (table 1), the data of the104 endometriosis patients were entered into a Microsoft Access database.

The operations were mostly laparoscopic and only in rare cases a laparotomy had to be performed. The localization (right/left ovary, uterus, parametrium, tube, pouch of douglas, bladder peritoneum, bladder mucosa, ureter, colon, rectum, rectovaginal septum, sacrouterine ligament, liver, peritoneum, vagina, extra-abdominal) and specifically the presence of endometriomas, (which in the literature is significantly associated with severe dysmenorrhea and pelvic pain [31, 32]) were also recorded. The number of the endometrial lesions (multiple, medium or sporadic) and the type of the endometrium lesions (superficial, infiltrated, or penetrated) and the appearance of adhesions were well documented.

The number and the date of each operation, as well as well as the stage of the endometriosis at each operation were recorded. A distinction was made between positive findings in the last operation and any previous operations.

In cases that the stage of endometriosis wasn't documented by the surgeon who performed the operation, an experienced gynecologist classified the operation reports according to the r-ASRM criteria based on the existing data (number, localization, size of lesion, presence of endometriomas and adhesions) in 4 categories: I (minimal), II (mild), III (moderate) and IV (severe).

4. 5. Data extraction and Statistical analysis

Microsoft Access was used for the collection and administration of the data. This was then imported into Microsoft Excel, where the relevant statistical analyses were carried out. Built-in excel toolkits correlated various variables via the Pearson product-moment coefficient**.** When the correlation coefficient (Pearson's correlation coefficient commonly represented by the Greek letter ρ) was in the range 0.1 to 1.0, the two variables were considered positively correlated. If the correlation coefficient was between -0.1 and -1.0, the variables were considered anti-correlated. If in-between, -0.1 to 0.1, no significant correlation was present.

The p-value was used, were necessary, to measure the deviation from randomness that a set of numbers exhibit and it was based on Chi-square-test. The p-value was characterized as "significant", when it was less than 0.05 and as “tendency” when between 0.05 and 0.1.

5. Results

Characteristics of the study collectives

208 women were included in this study: 104 endometriosis patients and 104 belonging to the control group. As expected, due to the matching criteria, the ages, the nationalities, and the education of the two groups didn't differ in any statistically significant way.

Distribution of pain group

The majority of chronic pain patients in the present study suffered from endometriosis - associated pain. The composition of our study participants with pain is summarized in figure 1.

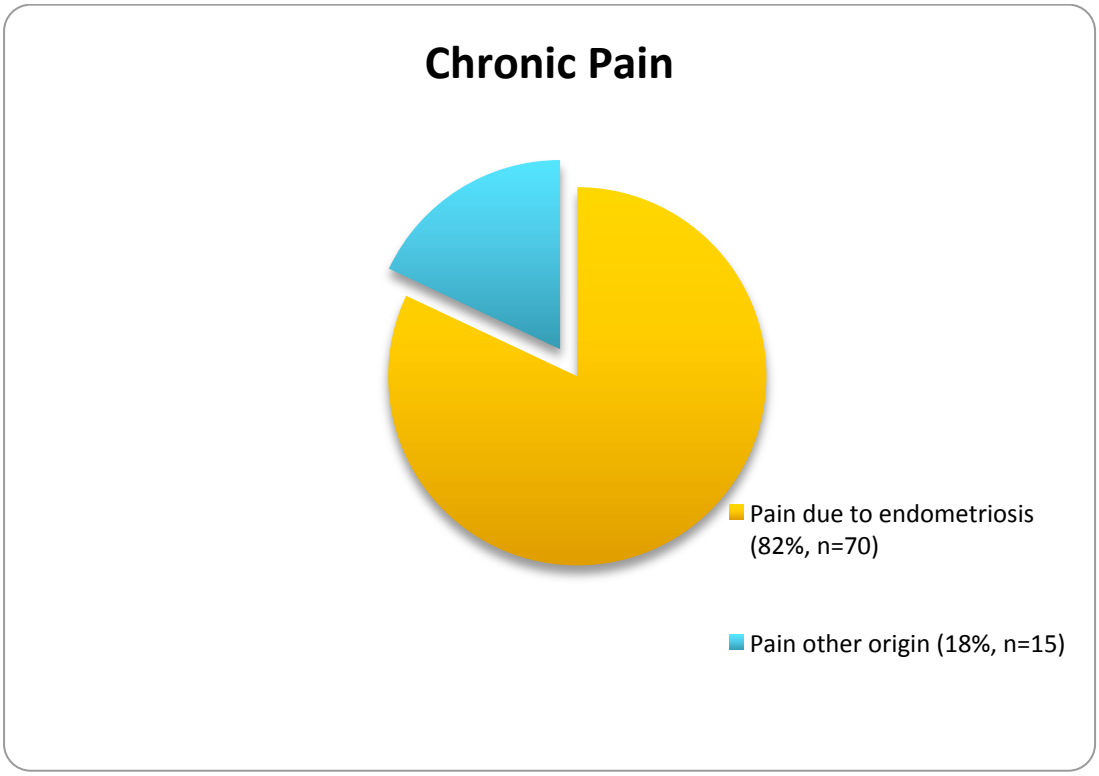

Fig. 1: Distribution of pain group (%)

Age

The average year of birth of people with endometriosis was 1971. In 2009, when the study took place, they were 38 years old. The oldest was 55 years old and the youngest 20. The SD (standard deviation) of the ages was 7.45 years.

The average year of birth of people in the control group was 1972. In 2009 they were 37 years old. The oldest was 57 years old and the youngest 18. The age difference between the two groups was not statistically significant (p-value = 0.054). The average age of all the participants was 37 years old.

In the following figure the participants were split up into five-year categories, figure 2.

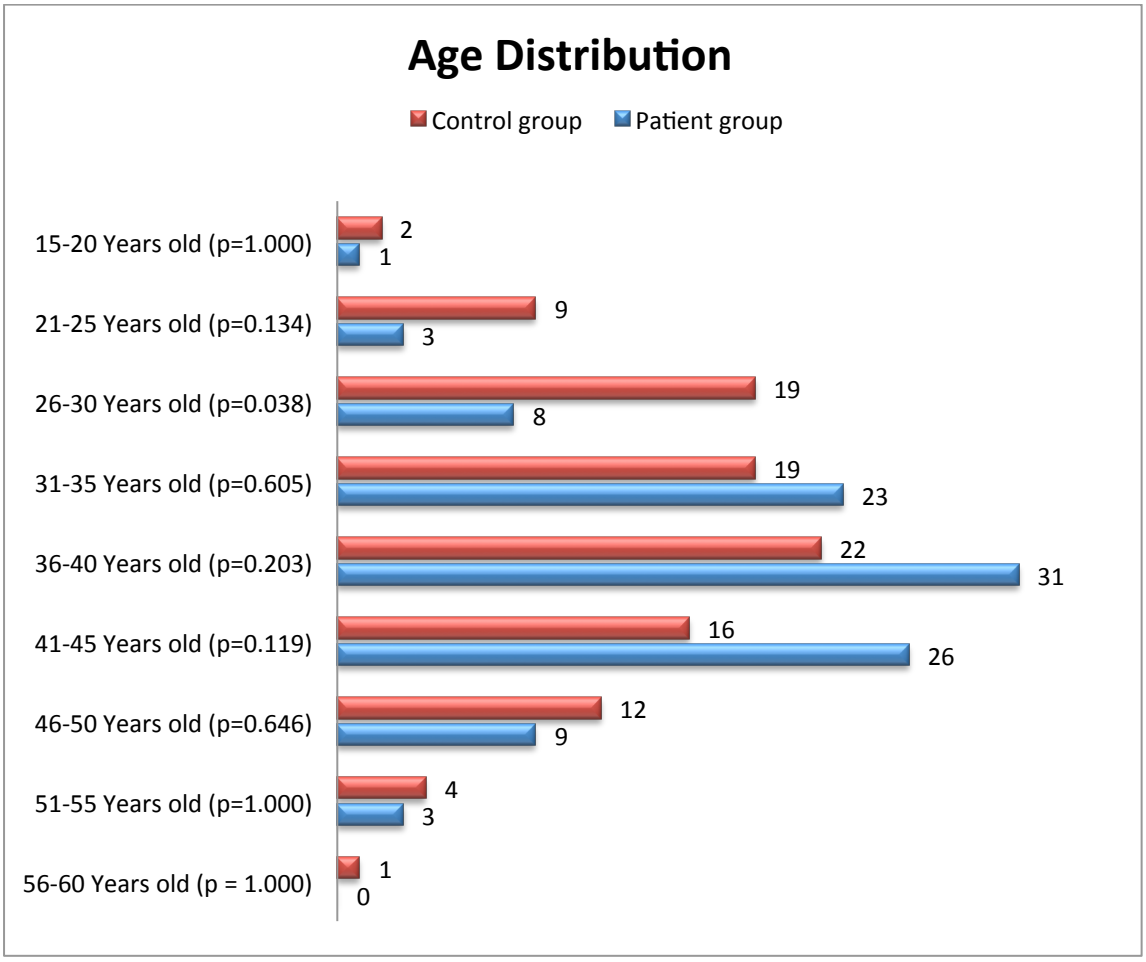

Fig. 2: Age distribution of participants (N)

Nationality

All the participants spoke German fluently. The majority of the participants came from Germany, and only a small minority came from a non-German speaking country. The nationality difference between the control and endometriosis group was not statistically significant ($\rho = 0.21$).

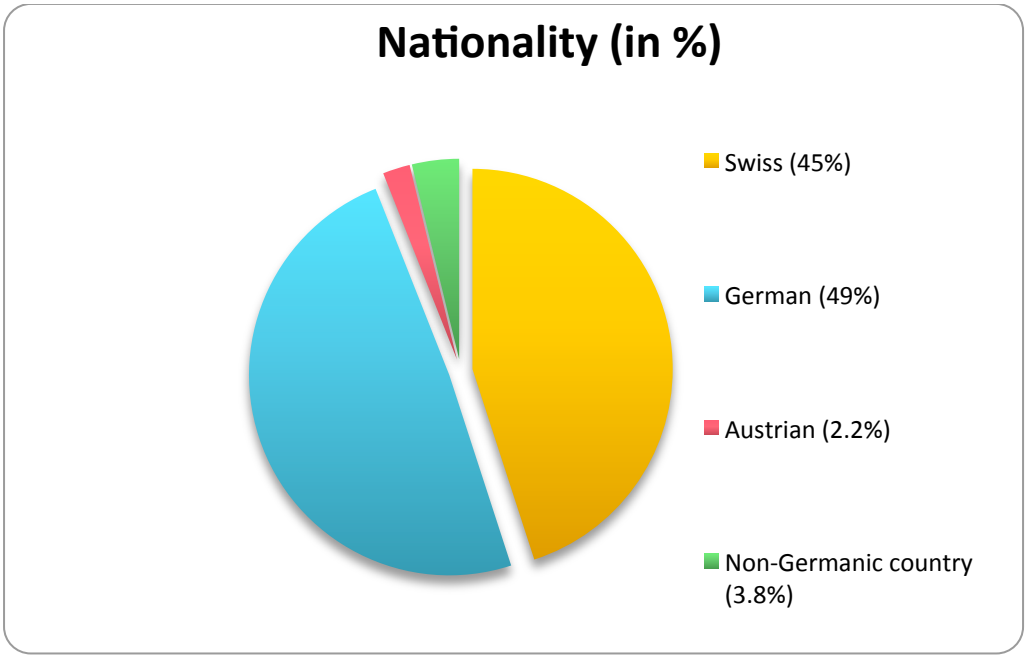

Fig. 3: Nationality of participants (%)

Education

To investigate the education status, education was divided into 3 categories: “high education”, “basic and low education” and “unclear”. The following table, table 4, shows the education status of the participants. Due to the matching between the control and the patient group, no significant differences were found.

	Patients (N = 104)	**Control-group** (N = 104)	**p-value**
High education	62.5% (65)	63.5% (66)	p = 1.000
Basic and low education	31.7% (33)	26.9% (28)	p = 0.543
Unclear status	5.8% (6)	9.6% (10)	p = 0.436

Tbl. 4: Education status of the participants

Civil status- Maternity status

There was no significant difference in the civil statuses of the two groups; the majority of the women of the endometriosis group were in a relationship (81.7% of the population with endometriosis) in comparison to 80.8% of the control group. There was no correlation between endometriosis and civil status with ρ = 0.012, p-value = 0.0855, Table 5.

Despite this, the majority of endometriosis patients had no children (77%), almost double than among the control group (39%). There was a high negative correlation between endometriosis and maternity with ρ = -0.34, Table 5, figure 4 and 5.

	Patients (N = 104)	**Control-group** (N = 104)	**p-value**
Married or in a long relationship	81.7% (85)	80.8% (87)	p = 0.855
Women with children	22.1% (23)	58.7% (61)	p = < 0.0001

Tbl. 5: Civil status and maternity status of the study participants (%)

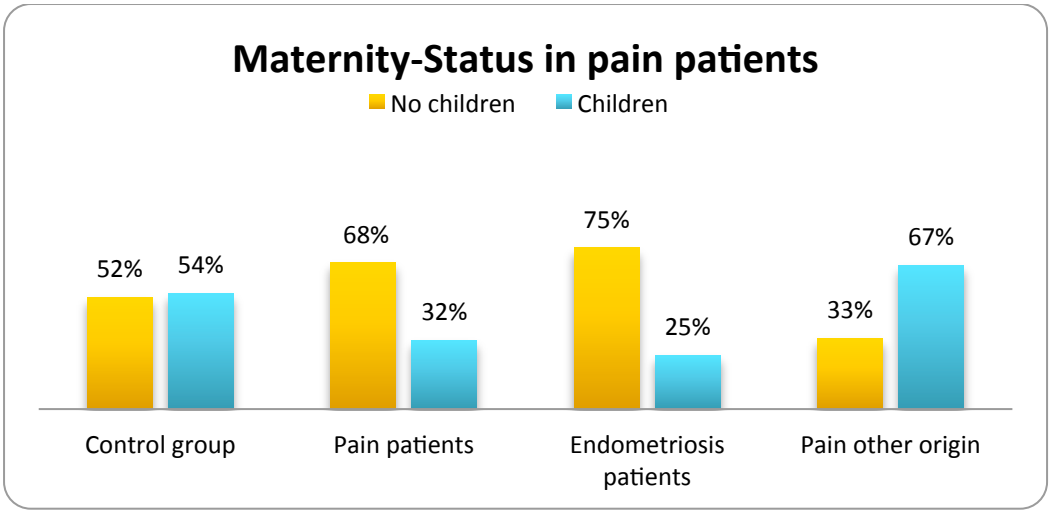

Fig. 4: Maternity status of the study participants (%)

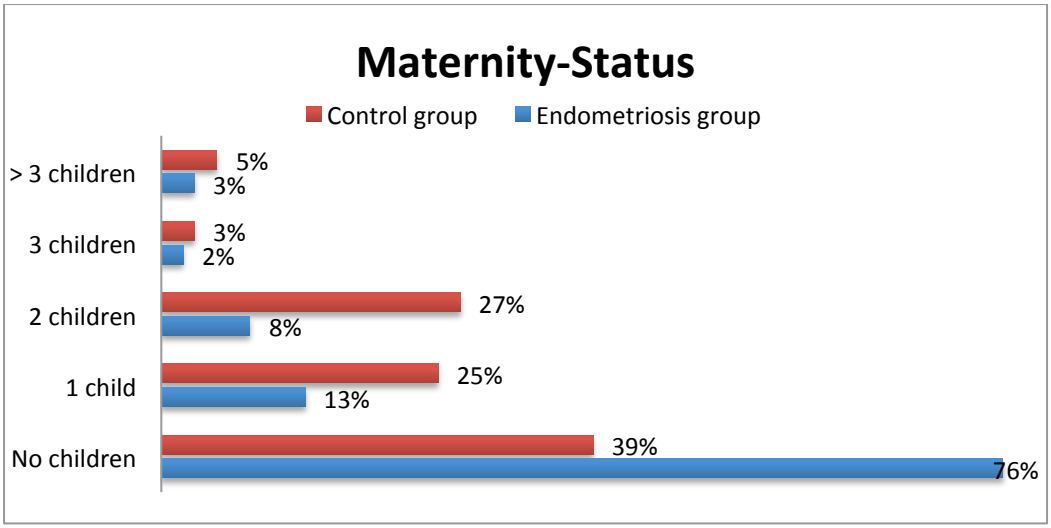

Fig. 5: Maternity status of the participants (%)

Lifestyle (BMI, diet, sports, smoking and drug habits) and pain

There was no correlation between the BMI and existence of pain (ρ = -0.04), see figure 6.

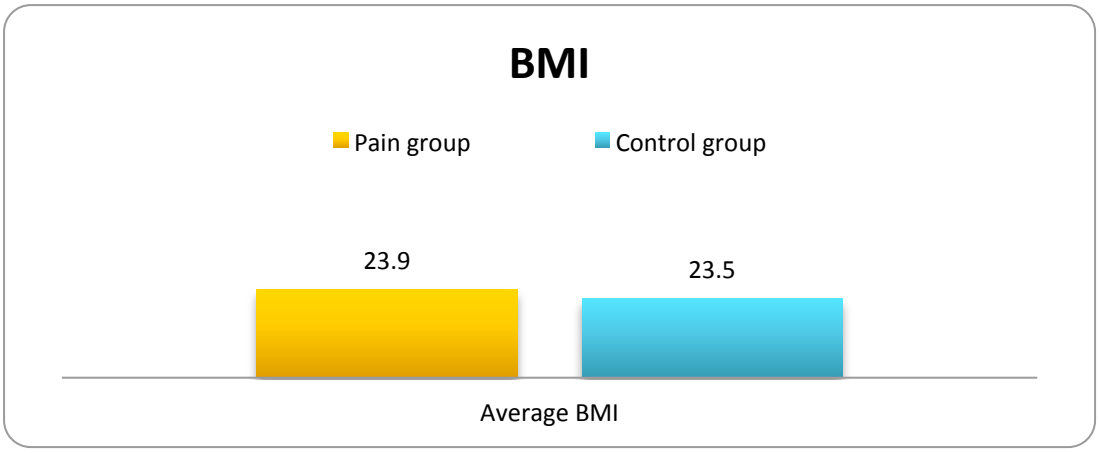

Fig. 6: BMI in pain group and control group

In our project there was no statistical significant difference concerning the nutritional habits (breakfast, consumption of dairy products, fruits, carbohydrates, fish and eggs and alcohol) between the pain group and the control group. The correlations (ρ) were all almost 0.
The only food categories that did show a non-zero correlation with endometriosis- associated pain, were between the consumption of vegetables (ρ =-0.12) and the consumption of beer (ρ =-0.12). There was a higher correlation between endometriosis - associated pain and the consumption of vegetables, as well as with the consumption of beer among these patients. This anti-correlation was rather minor.

There was also no significant difference between exercise sports between pain group and control group ($\rho = -0.09$), table 6.

There was also no correlation between smoking and the appearance of pain ($\rho = 0.012$), as well as drug consumption ($\rho = 0.07$), table 7.

	No sports	**3h/ week**	**3h - 6h/ week**	**> 6h/ week**
Pain group	26%	52%	21%	1%
Control group	28%	38%	29%	5%

Tbl. 6: Sport activities in pain patients and control group (%)

	Never	**Occasionally**	**Regularly (1-2 per week)**
Pain group	97%	2%	1%
Control group	98%	2%	0%

Tbl. 7: Drug consumption among pain patients and control group (%)

Professional life and pain

There was no correlation between having pain and having a professional occupation ($\rho = 0.031$), figure 7.

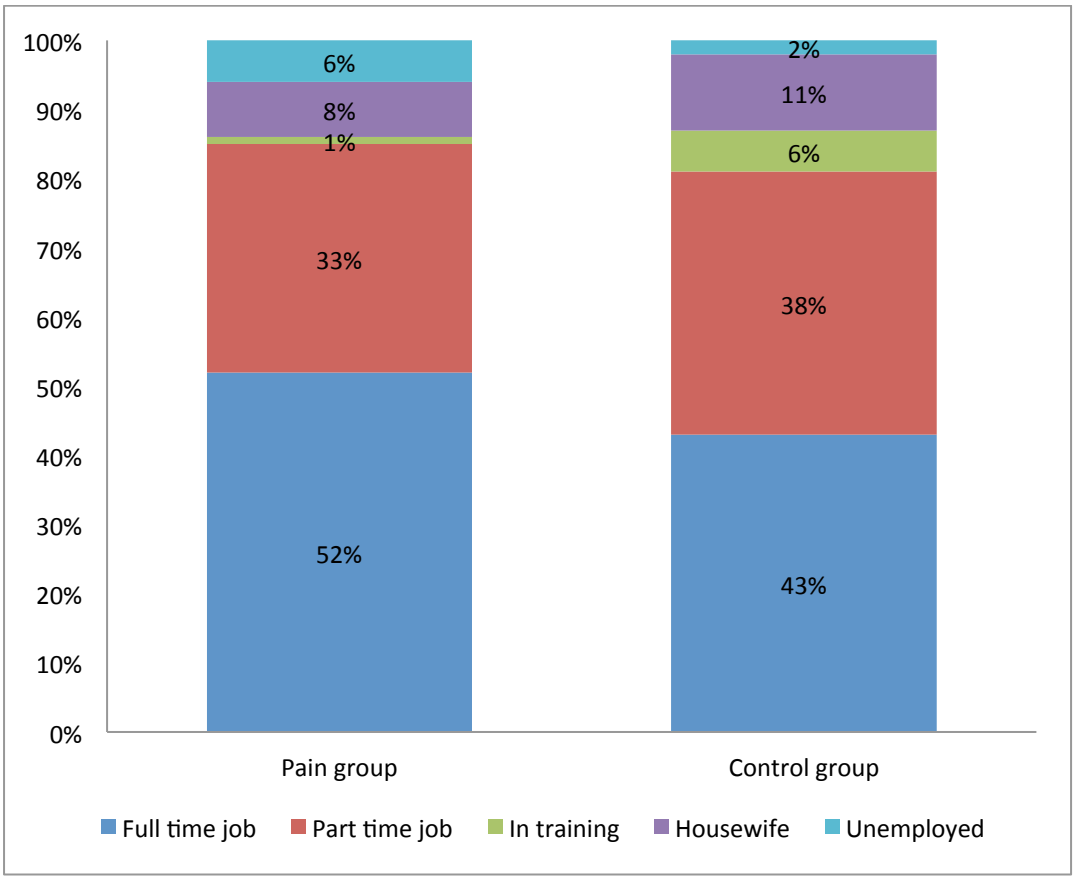

Fig. 7: Professional occupation in control und pain patients (%)

There was no correlation between the existence of pain and personal monthly income (ρ = -0.08), figure 8.

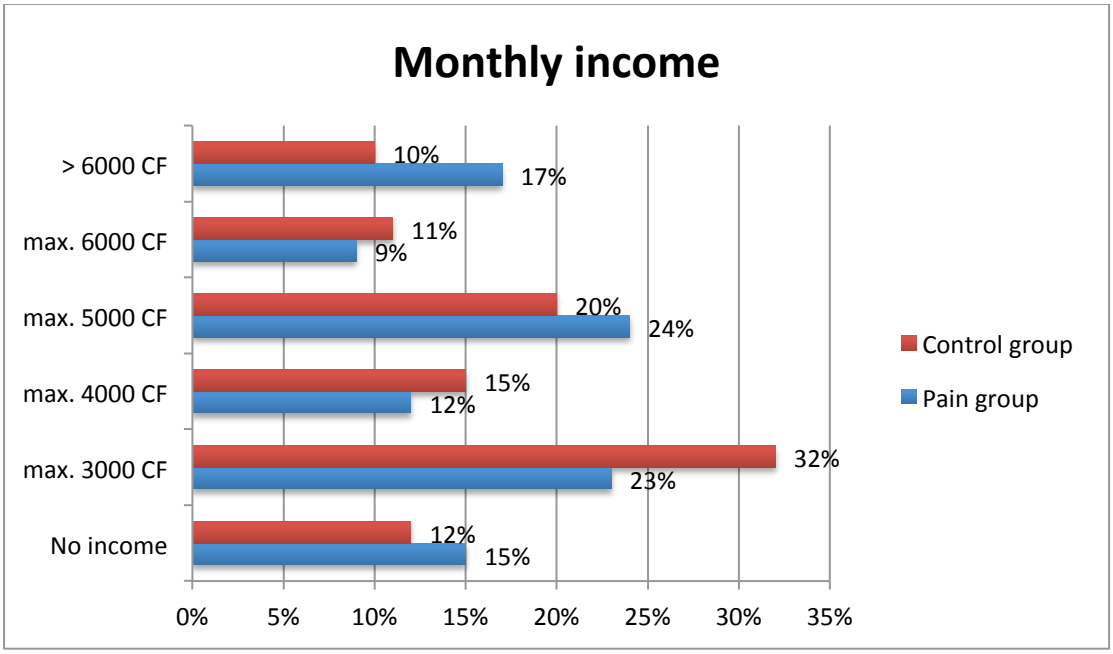

Fig. 8: Monthly income in pain patients and control group (%)

There was a slight positive correlation between pain and work experience (ρ = +0.11). There was also a correlation between pain because of endometriosis and work experience (ρ = 0.22). Patients with pain because of endometriosis had more working experience.

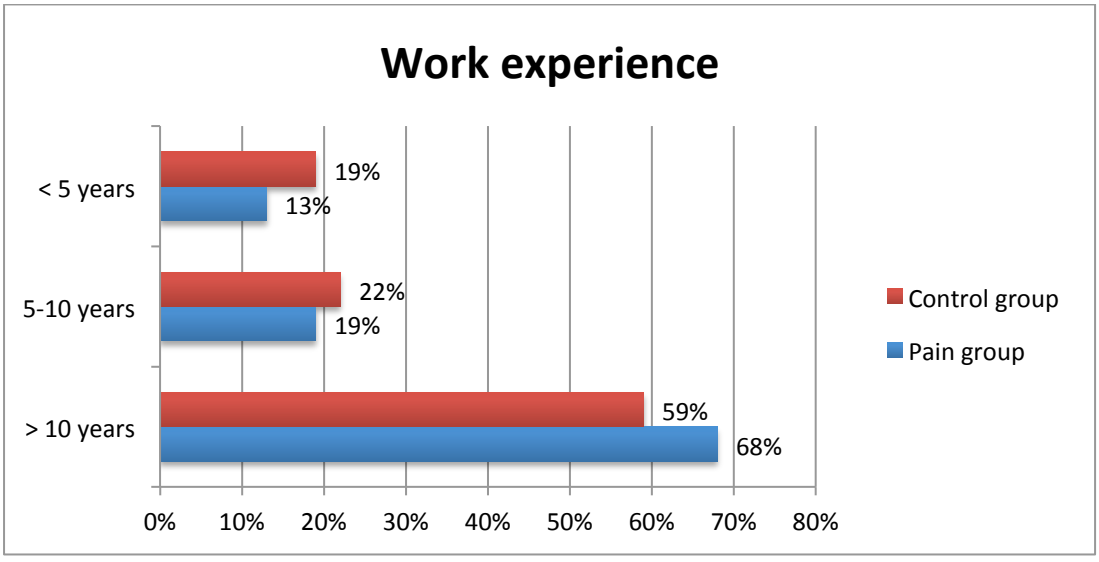

Fig. 9: Work experience among pain patients and the control group (%)

There was a weak positive correlation between existence of pain and stress at work, (ρ = 0.19). There was also a positive correlation between endometriosis patients with pain and stress in comparison to patients with pain of other origin (ρ = 0.16).

Pain group

The majority of our pain patients were women with endometriosis (N= 70). The distribution of our pain group was summarized in the figure 1, page 19. In the figure 10 we can also see the distribution of pain among the endometriosis patients.

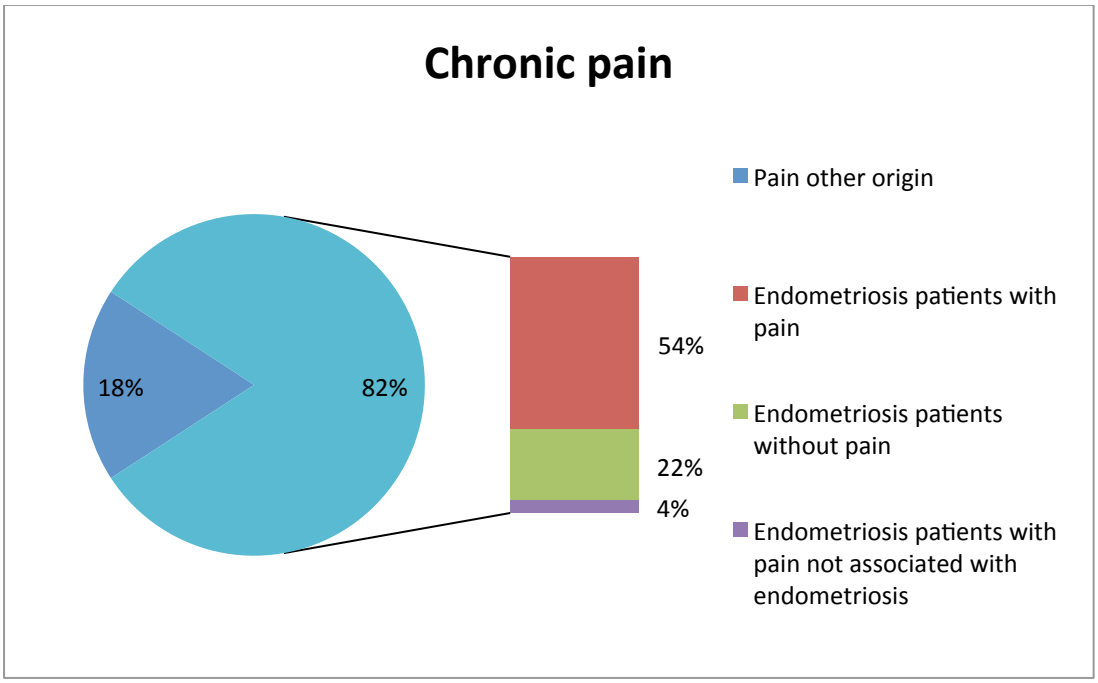

Fig. 10: Etiology of chronic pain among endometriosis patients (%)

Characteristics of pain group

In the following chapter we present the characteristics of the pain group from the perspective of the characteristics of endometriosis.

Endometriosis stage

The following figure shows the division of endometriosis stages according to the r-ASRM score, according to the last performed operation, detailed in table. 1. As summarized in figure 11, the majority of endometriosis patients were in stage IV. This corresponds to 44% of endometriosis patients.

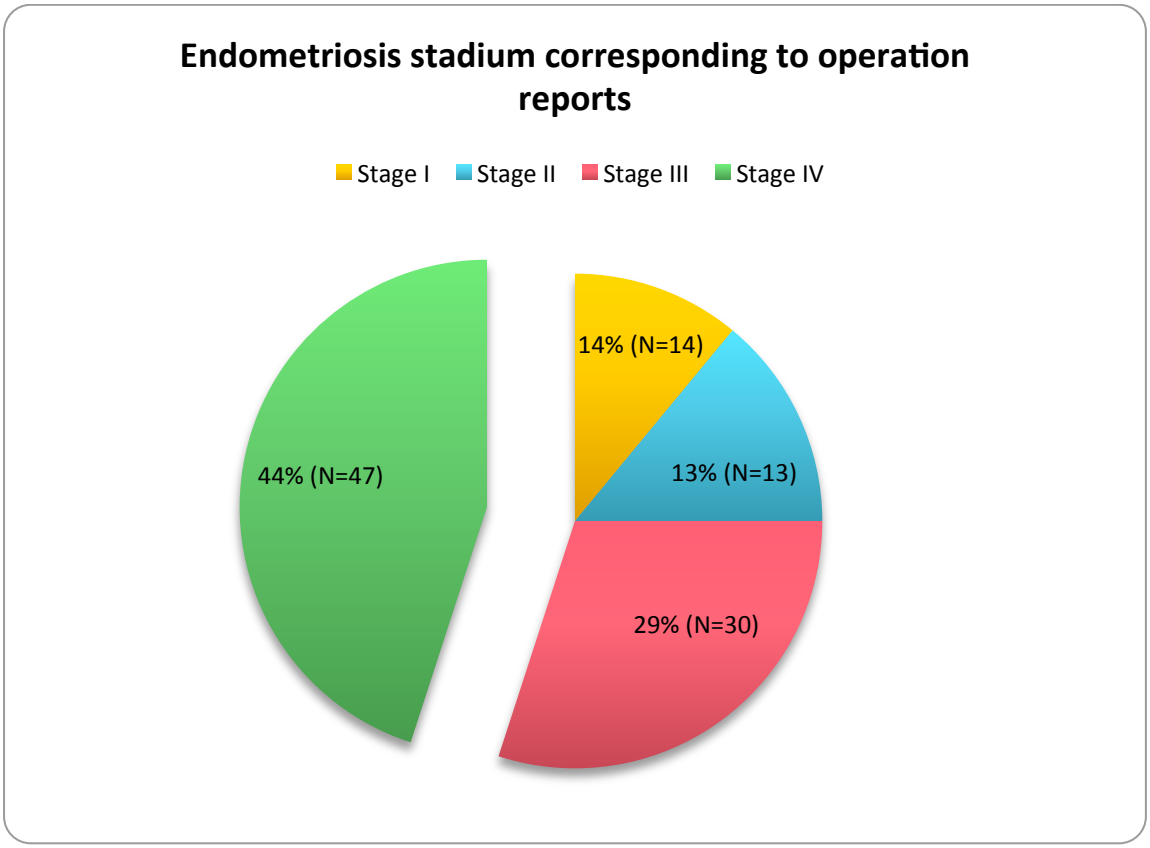

Fig. 11: Stage of endometriosis in endometriosis patients corresponding to the operations reports (%)

Number of operations

The majority of the patients with endometriosis, who had undergone operations because of endometriosis, had had one operation. As summarized in the figure and table below, the majority of endometriosis patients had had one or two operations (71% of endometriosis patients). The maximum number of operations that the patients went through was 7, which represented the 2% of endometriosis patients. See figure 12.

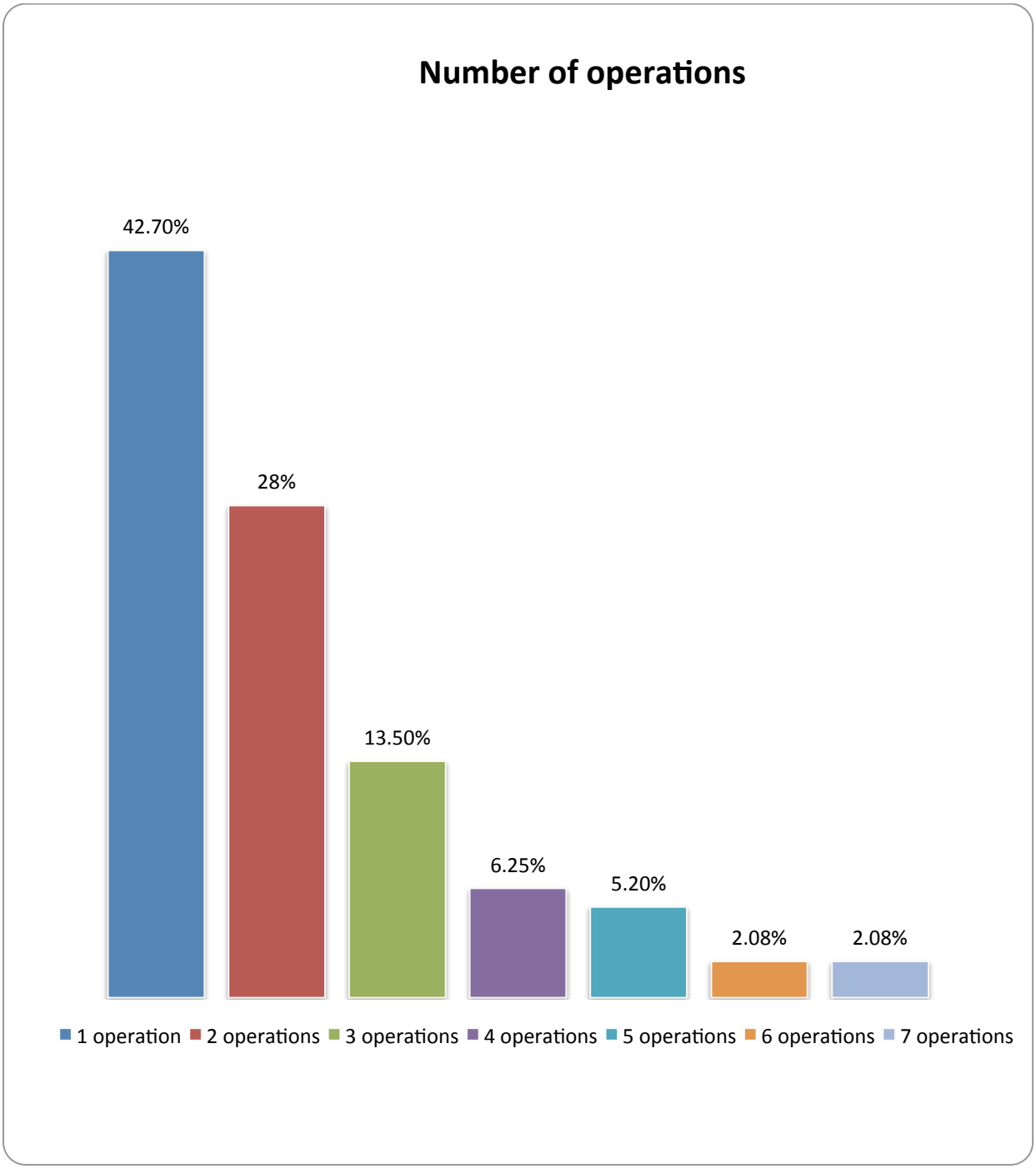

Fig. 12: Number of operations in endometriosis patients (%)

Location of endometriotic lesions

Figure 13 shows the location of endometriosis lesions as documented in the operation reports according to the last performed operation, for endometriosis patients. The most frequent lesion occurrence were those found in the Douglas pouch, and the next most frequent those found in the ovarian and the uterosacral ligaments.

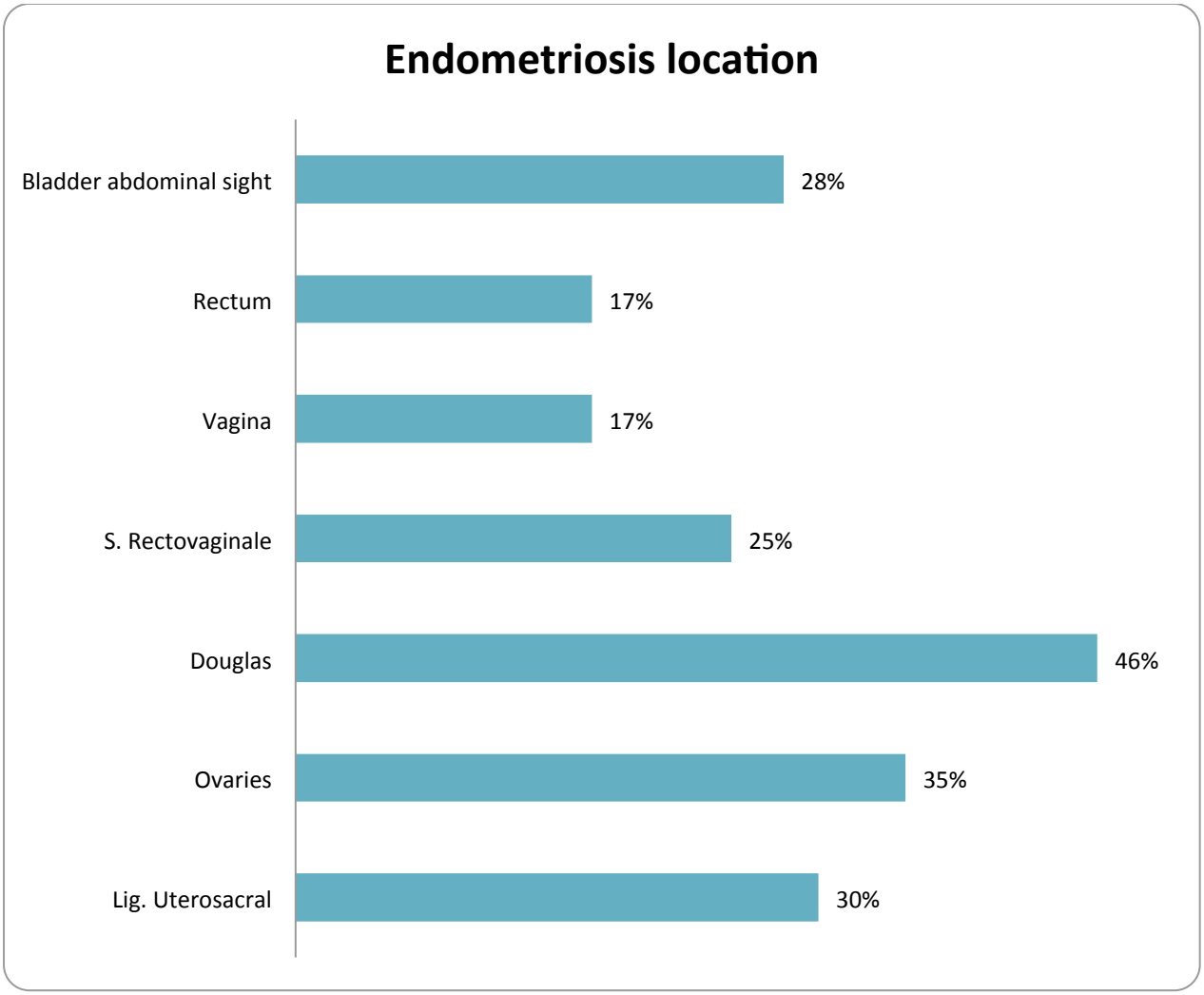

Fig. 13: Locations of endometriotic lesions in endometriosis patients corresponding to the operation reports (%)
S= Septum, Lig. = Ligamentum

Characteristics of pain in women with endometriosis - associated pain and women with pain of other origin

Location of pain

Endometriosis patients experienced abdominal pain nearly four times as often as women with pain of other origin. See figure 14.

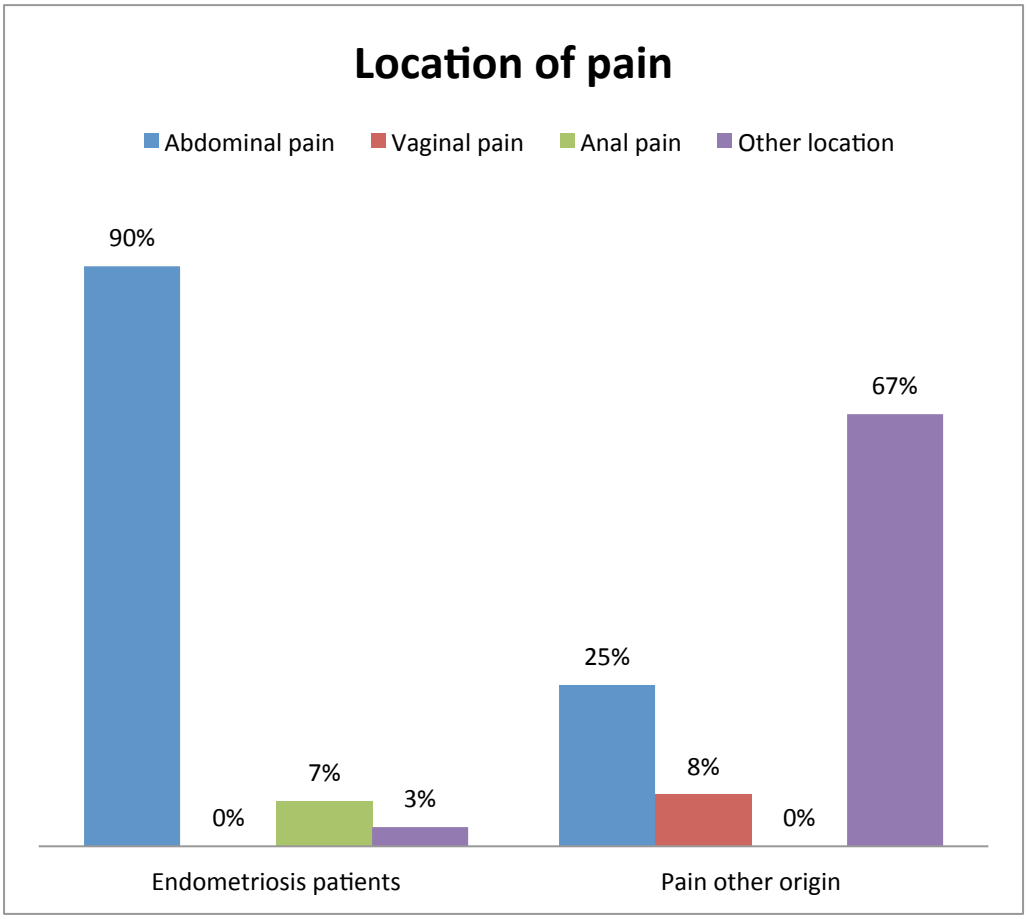

Fig. 14: Location of pain among pain patients (%). Other locations include the head, back and breasts.

Duration of pain

Endometriosis patients had pain for a longer portion of their lives than patients with chronic pain of a different origin with $\rho = 0.24$, figure 15. The majority of endometriosis patients had pain at least once over the past five years (76%) in comparison to 54% of pain other origin.

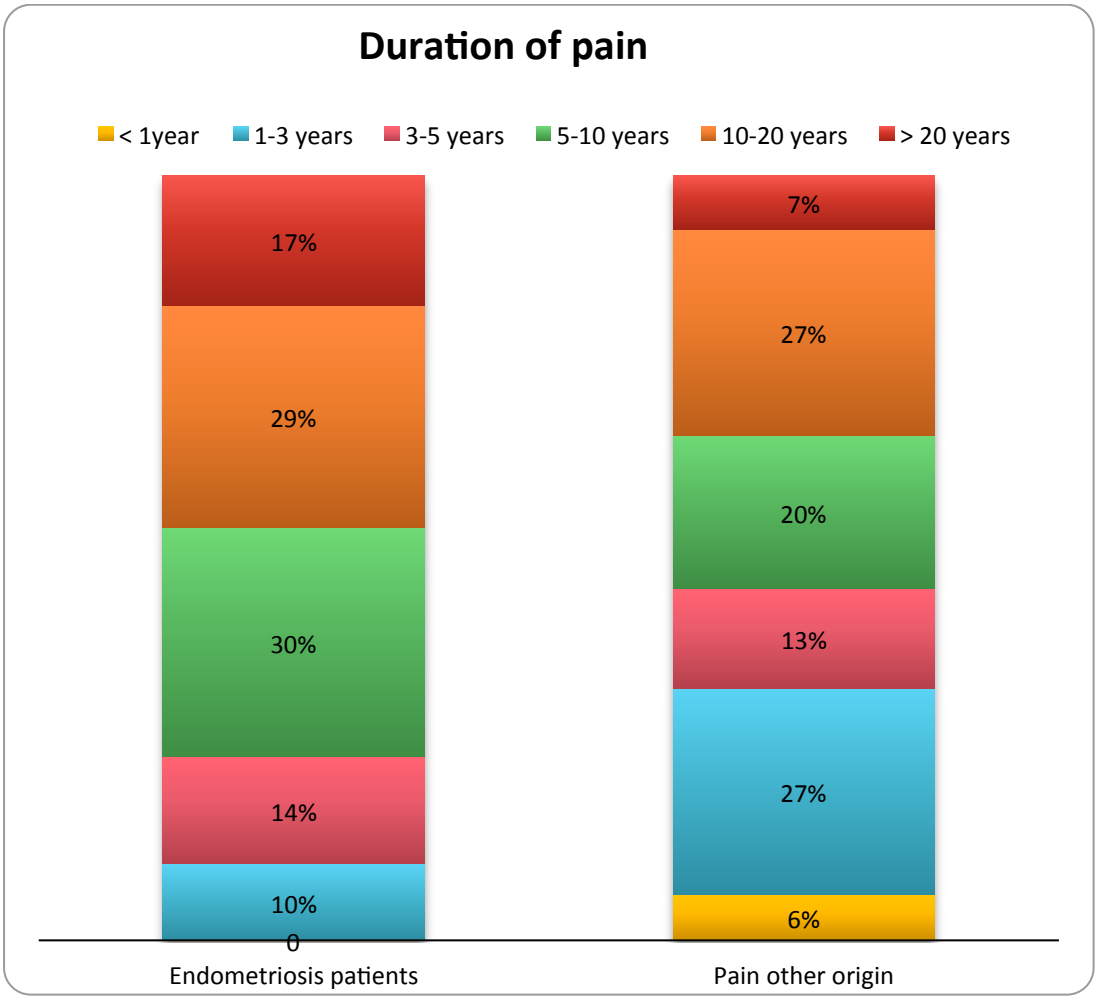

Fig. 15: Duration of pain in endometriosis and patients with pain other origin (%)

Frequency of pain

Pain was very frequent among pain patients, see figure 16. 77% of the endometriosis patients experienced pain at least once a week, in comparison to 85% of the participants with pain origin other than endometriosis (N = 14).

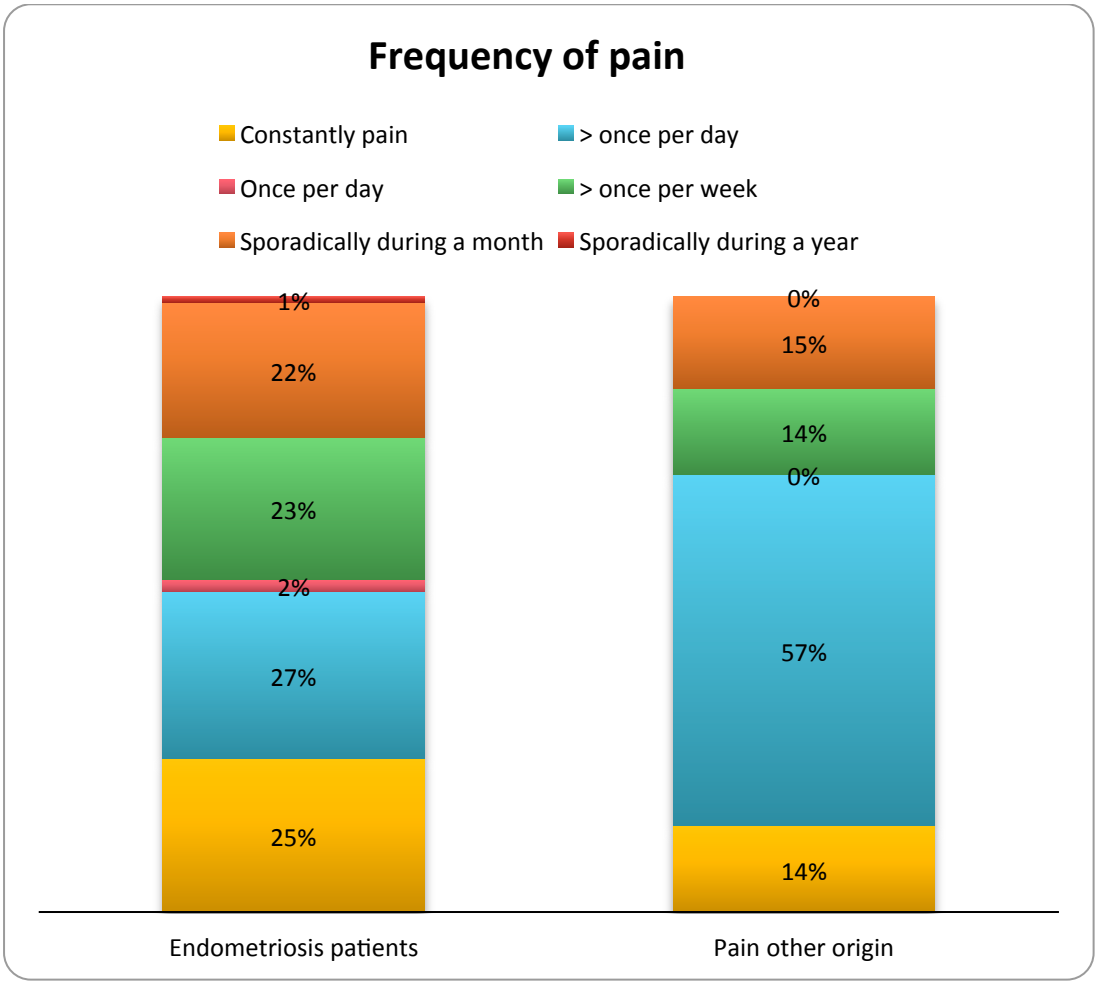

Fig. 16: Frequency of pain in endometriosis and patients with pain other origin (%)

The average duration of pain was 4-9 hours, and didn't differ significantly between the two groups, figure 17.

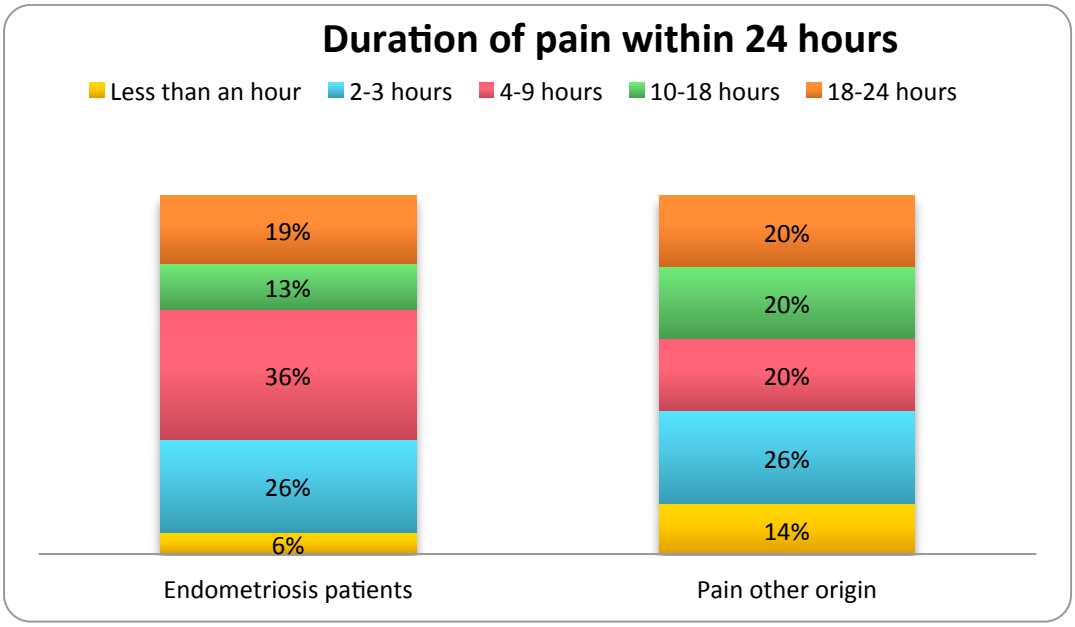

Fig. 17: Duration of pain within 24 hours in endometriosis and patients with pain other origin (%)

In women with endometriosis the pain was more often related to menstruation than in women with pain of other origin, figure 18.

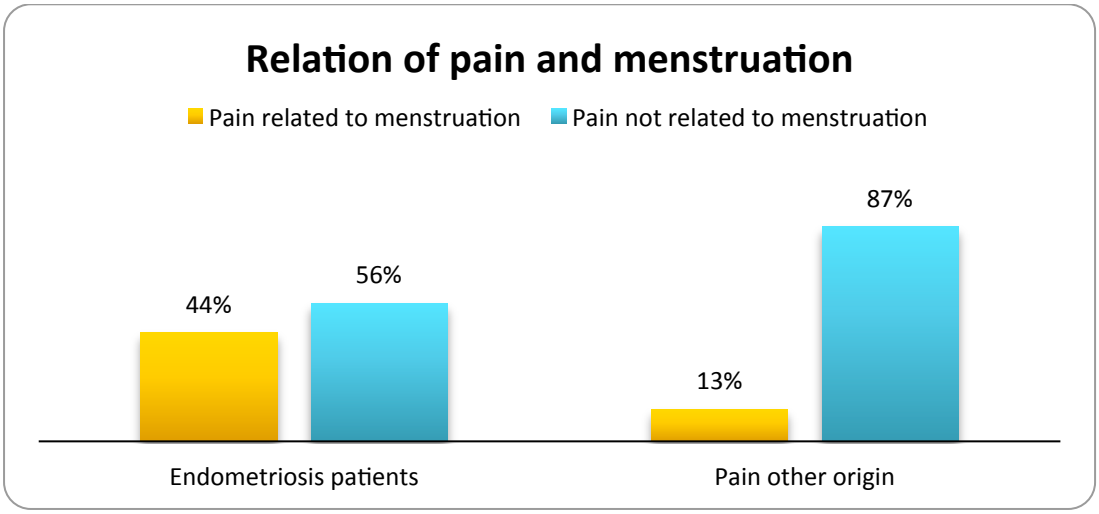

Fig. 18: Relation of pain to menstruation in endometriosis and patients with pain of other origin (%)

Intensity of pain

The mean maximal pain in endometriosis group was 4.78 on a scale from 0 to 10 in comparison to 4.26 among patients with pain other origin. However, 13% of endometriosis patients with pain scored more than 9 in the VAS in comparison to 0%, figure 19.

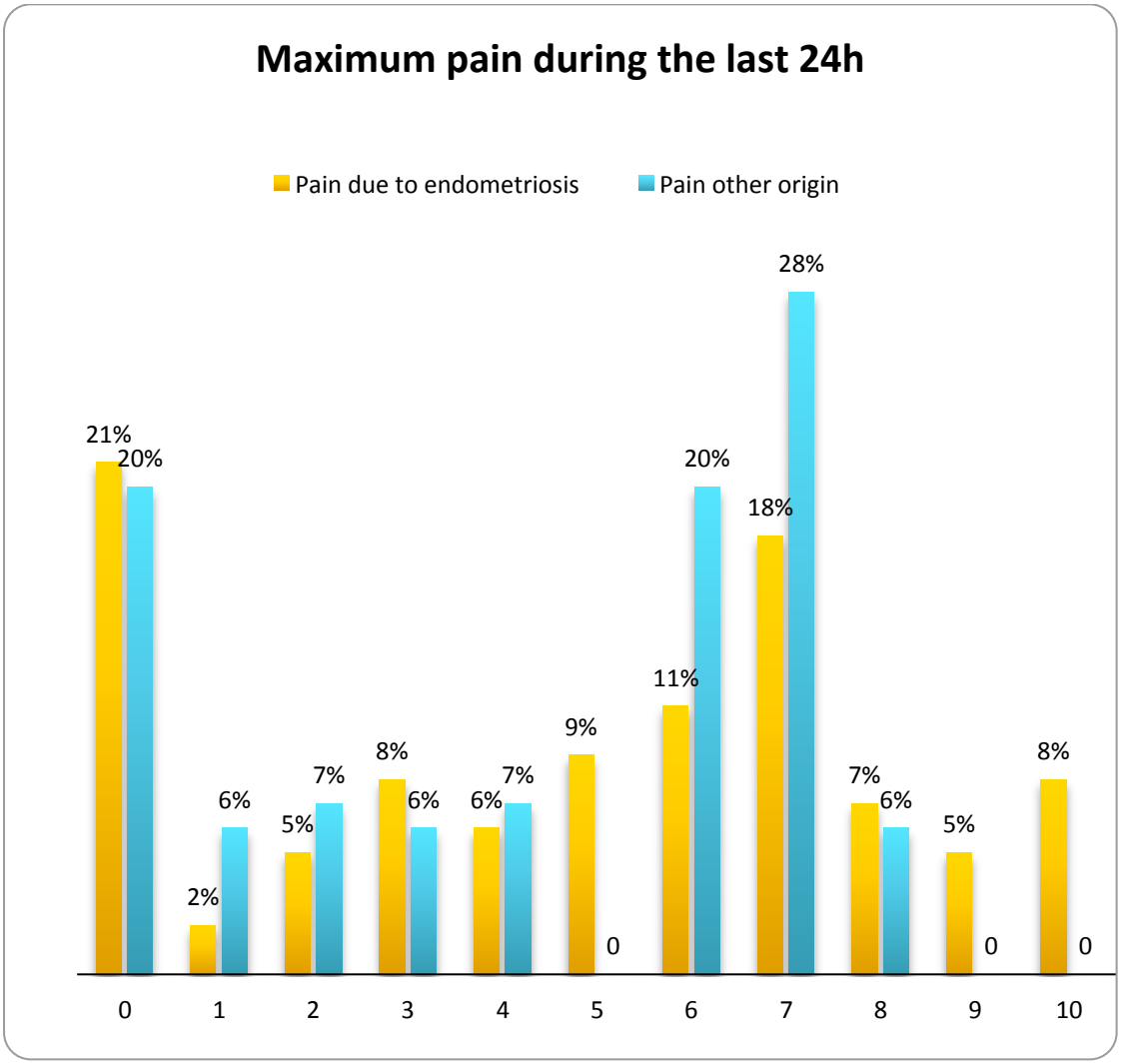

Fig. 19: Maximum pain in endometriosis patients and patients with pain of other origin (%)

The minimum pain over the last 24 hours also didn't differ between endometriosis patients and patients with pain other origin; endometriosis patients had a mean minimum pain of 1.88 in comparison to 1.93 among patients with pain other origin, figure 20.

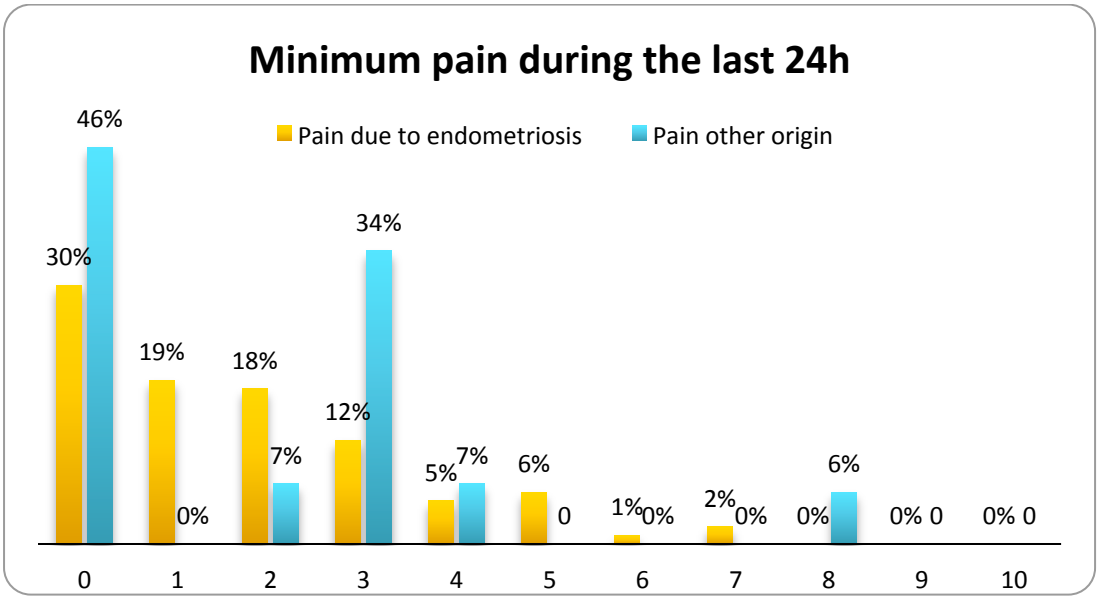

Fig. 20: Minimum pain in endometriosis patients and patients with pain of other origin (%)

The average pain during the last 24h didn't differ between endometriosis patients and patients with pain of other origin; the endometriosis patients had a mean average pain of 3.37 in comparison to 3.06 of patients with pain of other origin, figure 21.

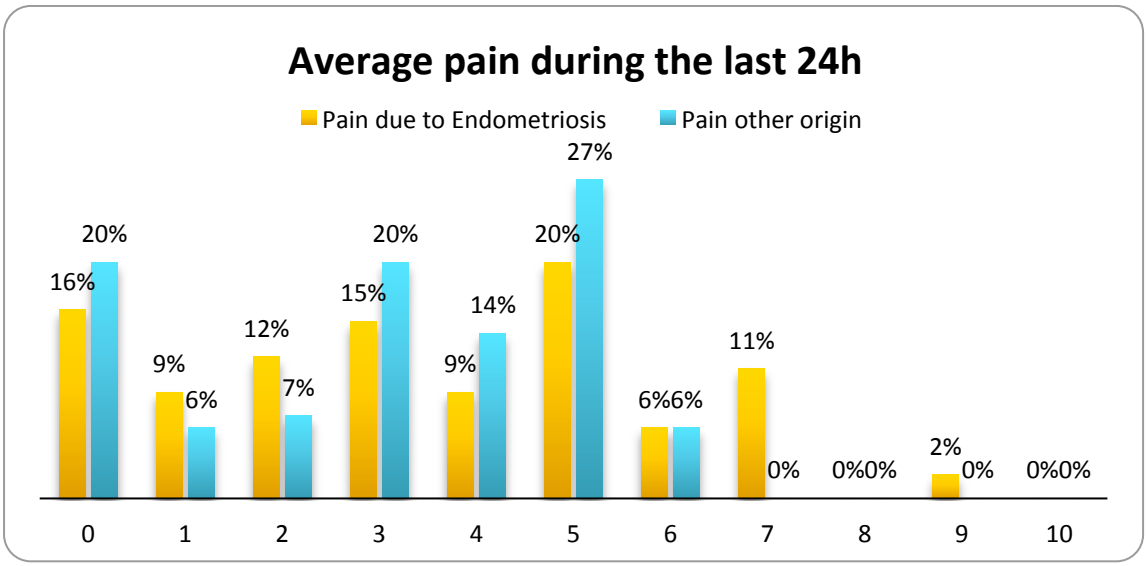

Fig. 21: Average pain during the last 24 hours in endometriosis patients and patients with pain of other origin (%)

The endometriosis patients gave an average pain of 3.03 in the VAS during the last month in comparison to 2.53 of the patients with pain of other origin, figure 22.

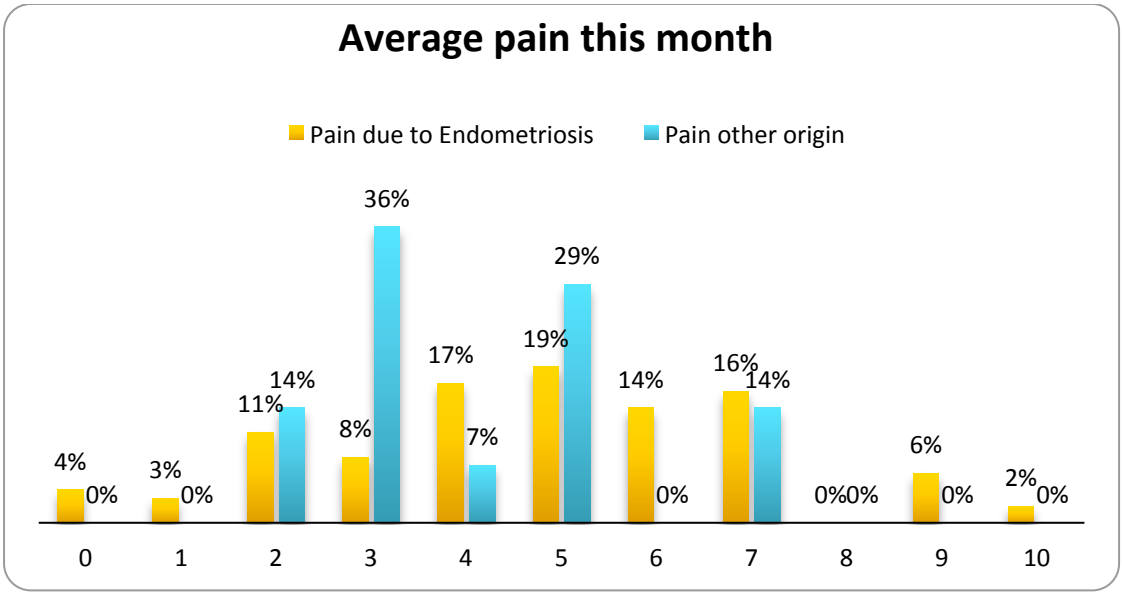

Fig. 22: Average pain this month in endometriosis patients and patients with pain of other origin (%)

As show in the figures above, the difference regarding the average pain between the two groups was not statistically significant ($p > 0.05$) and the average pain for each category didn't differ significantly between the two groups. The following figure summarizes the mean maximum pain level, minimum pain level and current pain level between endometriosis patients and patients with pain other origin, figure 23.

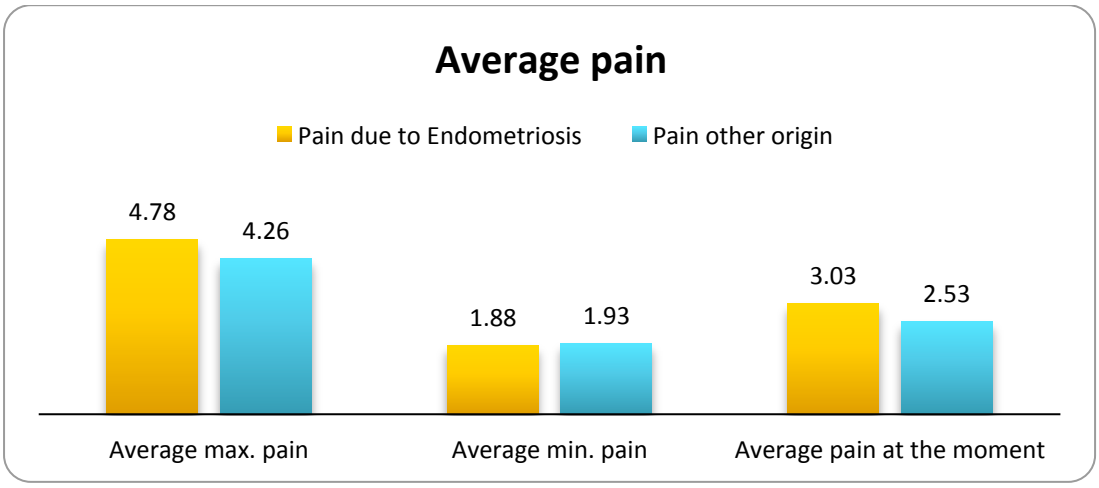

Fig. 23: Mean pain levels in endometriosis patients and patients with pain of other origin (%)

Neither endometriosis patients nor the patients with pain of other origin found total relief from their medication, see figure 24.

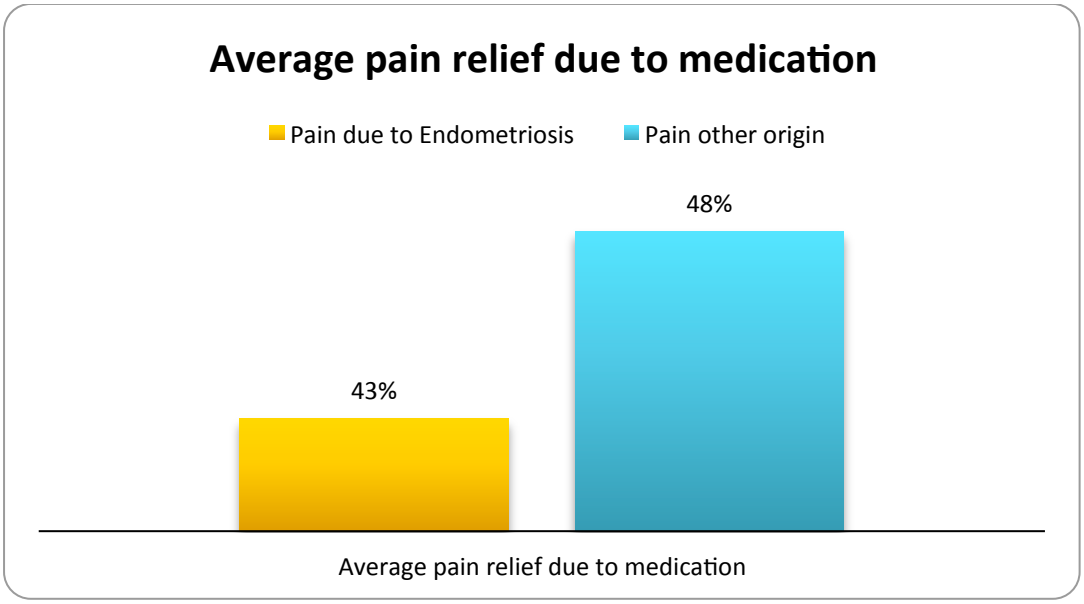

Fig. 24: Average pain relief due to medication over the last 24 hours in endometriosis patients and patients with pain of other origin (%)

Impact of pain

The effect of pain on their daily lives among endometriosis patients was higher than for patients with pain of a different origin. Patients with endometriosis had more difficulties to perform essential life activities like urinating and defecating. There was also greater impact in social activities among the endometriosis patients than among patients with chronic pain other origin, see figure 25**.** The differences between the two groups weren't statistically significant, tables 8 and 9.

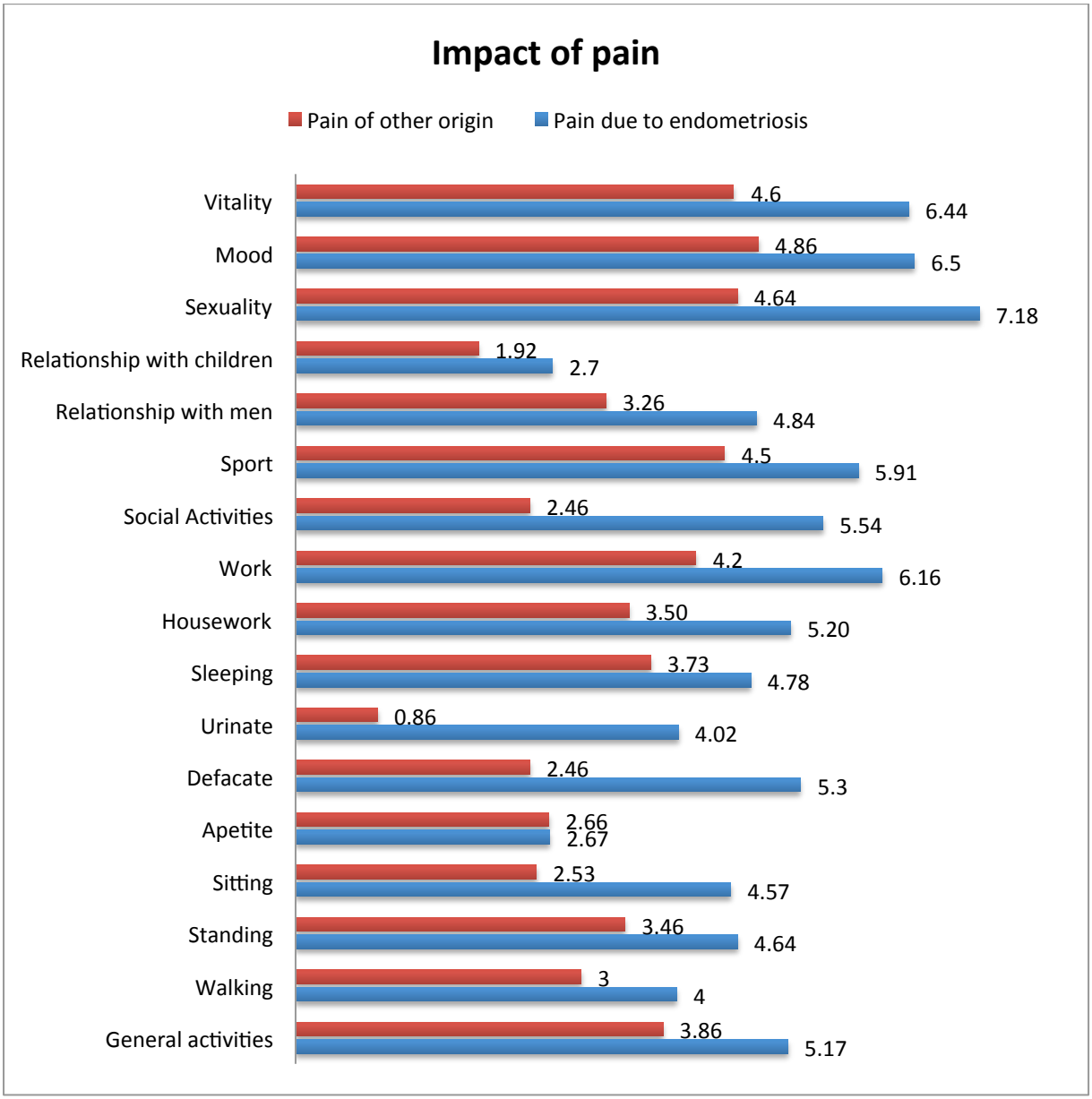

Fig. 25: Impact of pain in endometriosis patients and patients with pain of other origin (scale from 0-10)

	General Activities	Work	Social activities	Sport	Relationship with men	Relationship with children
p- value	0.86	0.32	0.18	0.43	0.17	0.80

Table 8: p- values of impact of pain by the endometriosis pain group and group of pain of other origin

	Sleeping	Housework	Sexuality	Free time	Mood
p- value	0.37	0.16	0.36	0.06	0.005

Table 9: p- values by impact of pain in the endometriosis pain group and group of pain of other origin

Stage of endometriosis and characteristics of pain

We found no correlation between the stage of endometriosis and the pain´s characteristics (intensity, duration, frequency). In the tables below (tables 10-13) we present different characteristics of pain corresponding to different stages of endometriosis.

There was no correlation between the stage of the endometriosis and the frequency of pain, with $\rho = 0.04$.

Frequency of pain	**never**	**< 1 per year**	**few times per month**	**many times per week**	**once per day**	**more times per day**	**constant**
Stage I	4%	0	0	3%	0	1%	3%
Stage II	6%	0	1%	3%	0	1%	2%
Stage III	9%	0	5%	7%	0	6%	3%
Stage IV	10%	1%	10%	5%	1%	12%	8%

Tbl. 10: Stage of the endometriosis and frequency of the pain

There was no correlation between the stage of the endometriosis and the duration of pain, with $\rho = 0.05$.

Duration of pain	**never**	**< 1 hour**	**2-3hours**	**4-9hours**	**10-18h**	**18-24h**
Stage I	2%	0	3%	2%	1%	2%
Stage II	6%	0	2%	4%	0	1%
Stage III	8%	4%	5%	4%	3%	5%
Stage IV	7%	3%	11%	14%	4%	4%

Tbl. 11: Stage of endometriosis and duration of pain

There was no correlation between the average pain over the 4 weeks leading up to the questionnaire (VAS) and the stage of endometriosis, with $\rho = 0.02$.

Pain over the last four weeks (rating on VAS scale)	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Stage I	3%	0	0	0	1%	3%	2%	2%	0	0	0
Stage II	6.5%	0	1%	1%	1%	2%	1%	0	0	0	0
Stage III	7.5%	1%	2%	3%	4%	2%	2%	3%	0	1%	1%
Stage IV	12%	1%	5.5%	3%	6.5%	6.5%	4%	5.5%	0	2%	0

Tbl. 12: Stage of endometriosis and results of pain rated on a VAS over the 4 weeks leading up to the questionnaire

There was no correlation between the pain at the time answering the questionnaire and the stage of endometriosis, with $P = 0.01$.

Pain at the moment (rating on a VAS scale)	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Stage I	3%	1%	1%	3%	0%	1%	1%	0	0	1	0
Stage II	8%	1%	1%	0	1%	2%	0	0	0	0	0
Stage III	16%	4%	3%	1%	1%	2%	1%	1%	0	0	0
Stage IV	23%	3%	1%	6%	3%	1%	5%	4%	0	5%	1%

Tbl. 13: Stage of endometriosis and results of pain rated on a VAS at the time of answering the questionnaire

Intensity of pain and adhesions

We found a low positive correlation between the intensity of the pain and the existence of adhesions with $\rho = 0.2$, figure 26. Patients with extended adhesions scored higher on VAS, designed to evaluate pain intensity.

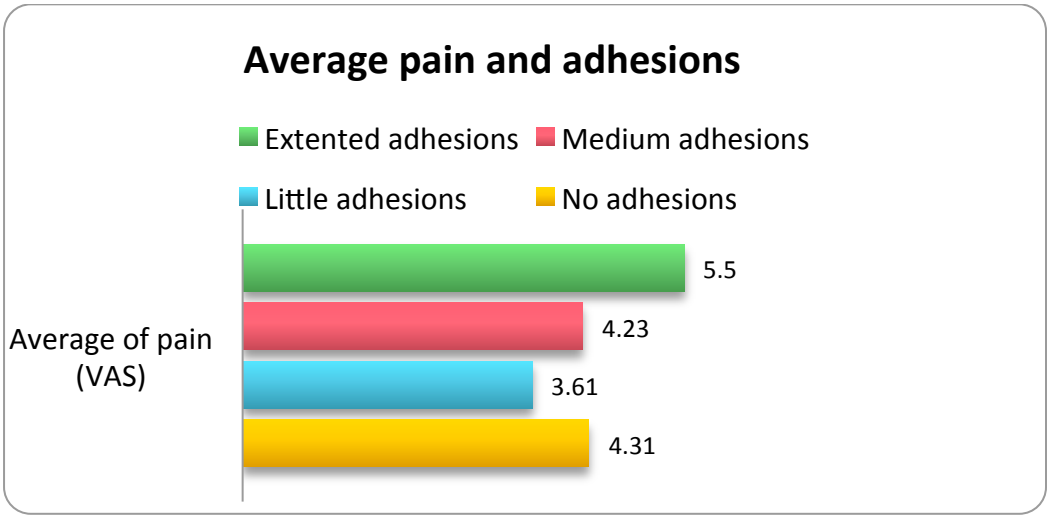

Fig. 26: Average pain in the last 4 weeks and the appearance of adhesions (VAS scale from 0-10)

Intensity of pain and type of adhesions

There was a low positive correlation between the intensity of pain and the type of adhesion. Dense adhesions were associated with more intense pain than tender adhesions with $\rho = 0.23$, figure 27.

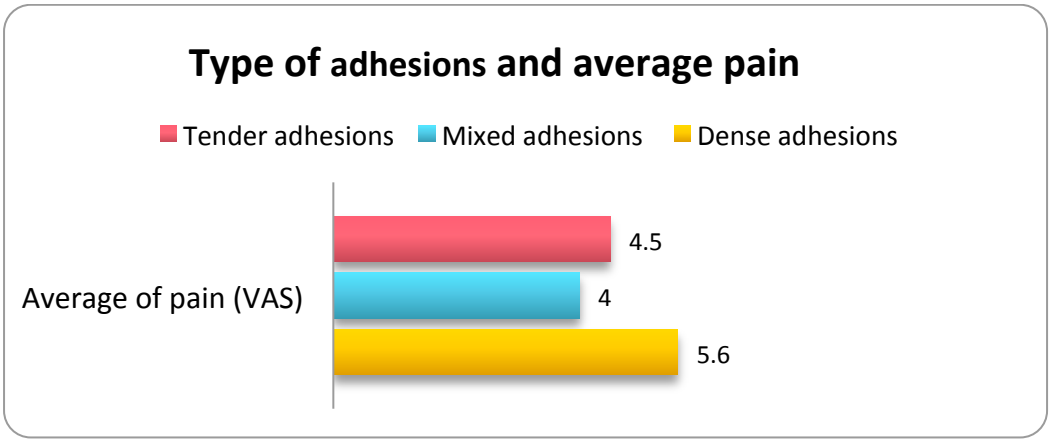

Fig. 27: Average pain in the last 4 weeks and type of adhesions (VAS scale from 0-10)

Intensity of pain and location of lesions

No correlation was found between the intensity of pain and the location of endometriosis lesions. In the following figure we can see the average pain in correlation to the anatomical places that in literature had been correlated with aggravation of pain and dysmenorrhea. 64 endometriosis patients answered this question. These results are according to the last operation.

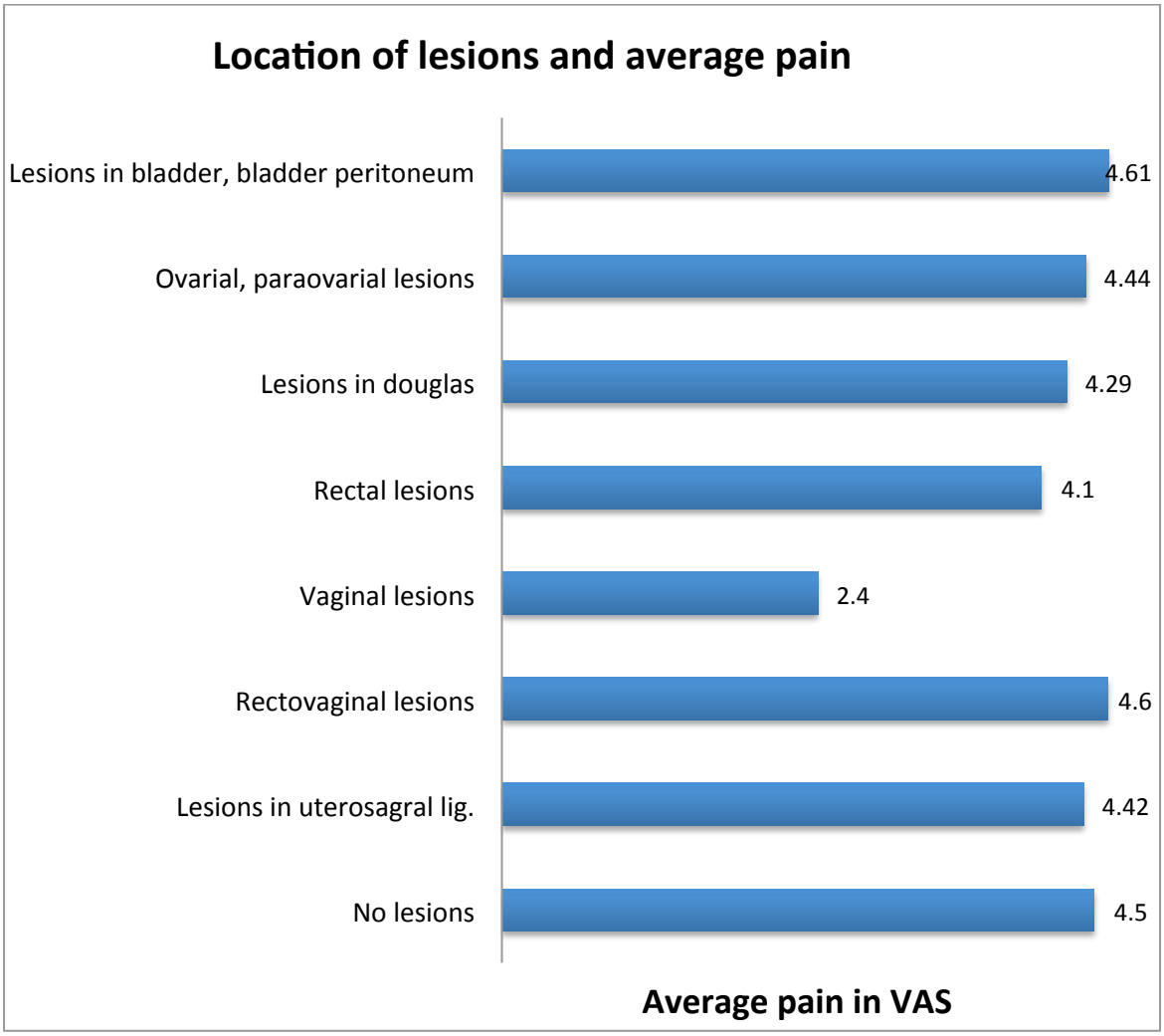

Fig. 28: Average pain in the last month and location of lesions (VAS scale from 0-10)

More specifically: There was no correlation with intensity of pain the month prior to taking the questionnaire, and for example the existence of adhesions in the uterosacral ligament, with $\rho = -0.02$. There was also no correlation between the intensity of pain and the existence of lesions in the rectovaginal septum ($\rho = 0.04$), vaginal ($\rho = 0.08$), rectal ($\rho = -0.07$), in the Douglas pouch ($\rho = -0.09$), ovarial or para-ovarial ($\rho = -0.02$) nor in bladder and bladder peritoneum ($\rho = 0.01$).

Intensity of pain and type of endometrial lesions

In our study neither the number nor the depth of the endometrial lesions were correlated with the intensity of pain. However there was a low correlation between the intensity of the pain and the size of the endometrial lesions. Based on our study the bigger the lesion (>3cm) was, the more intense was the pain ($\rho = 0.14$), figure 29. Note that the size of the endometriosis group who answered the following question was limited (N=31).

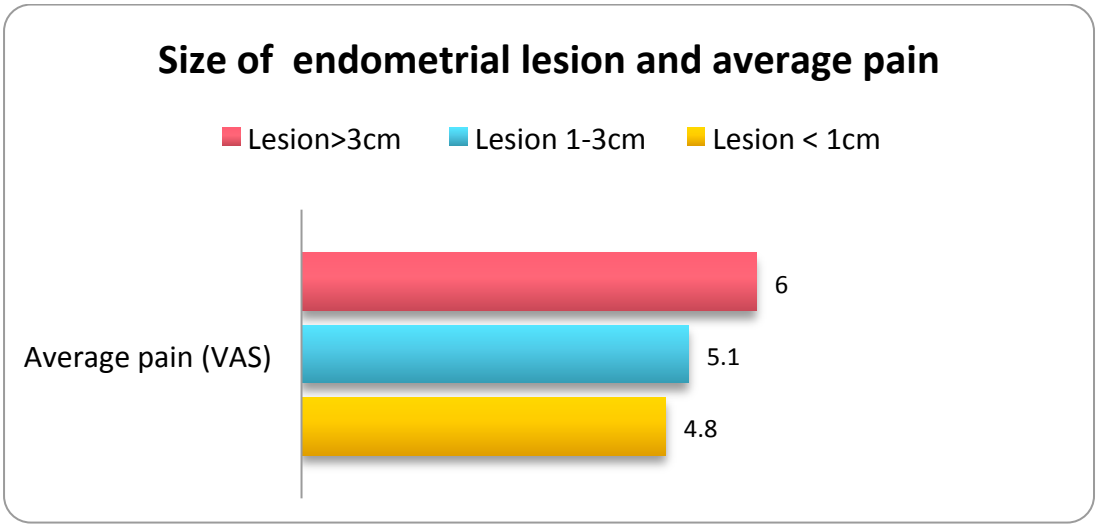

Fig. 29: Average pain over the last month and size of endometrial lesions (VAS scale from 0-10)

There was no correlation between the intensity of pain the previous month and the existence of single in comparison to multiple endometriosis lesions, ($\rho = -0.01$).

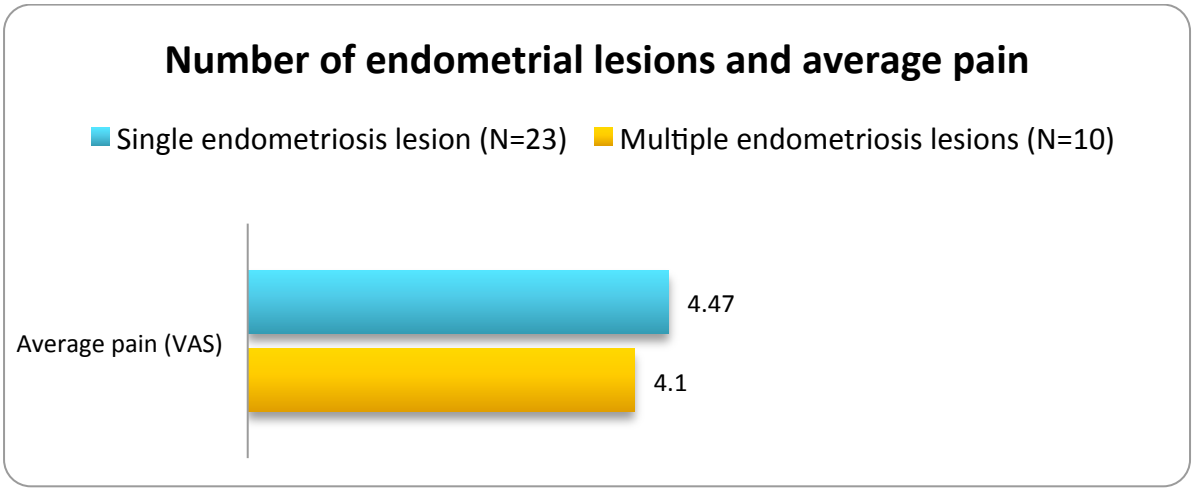

Fig. 30: Average pain last month and number of endometrial lesions (VAS scale from 0-10)

There was no correlation between the intensity of pain and the presence of infiltrating endometrial lesions either on the uterosacral ligament, ($\rho = -0.06$), or rectrovaginal ($\rho = -0.03$), or in rectum ($\rho = -0.07$. There was no correlation between the average pain and the presence of superficial or infiltrating endometrial lesions, figure 31.

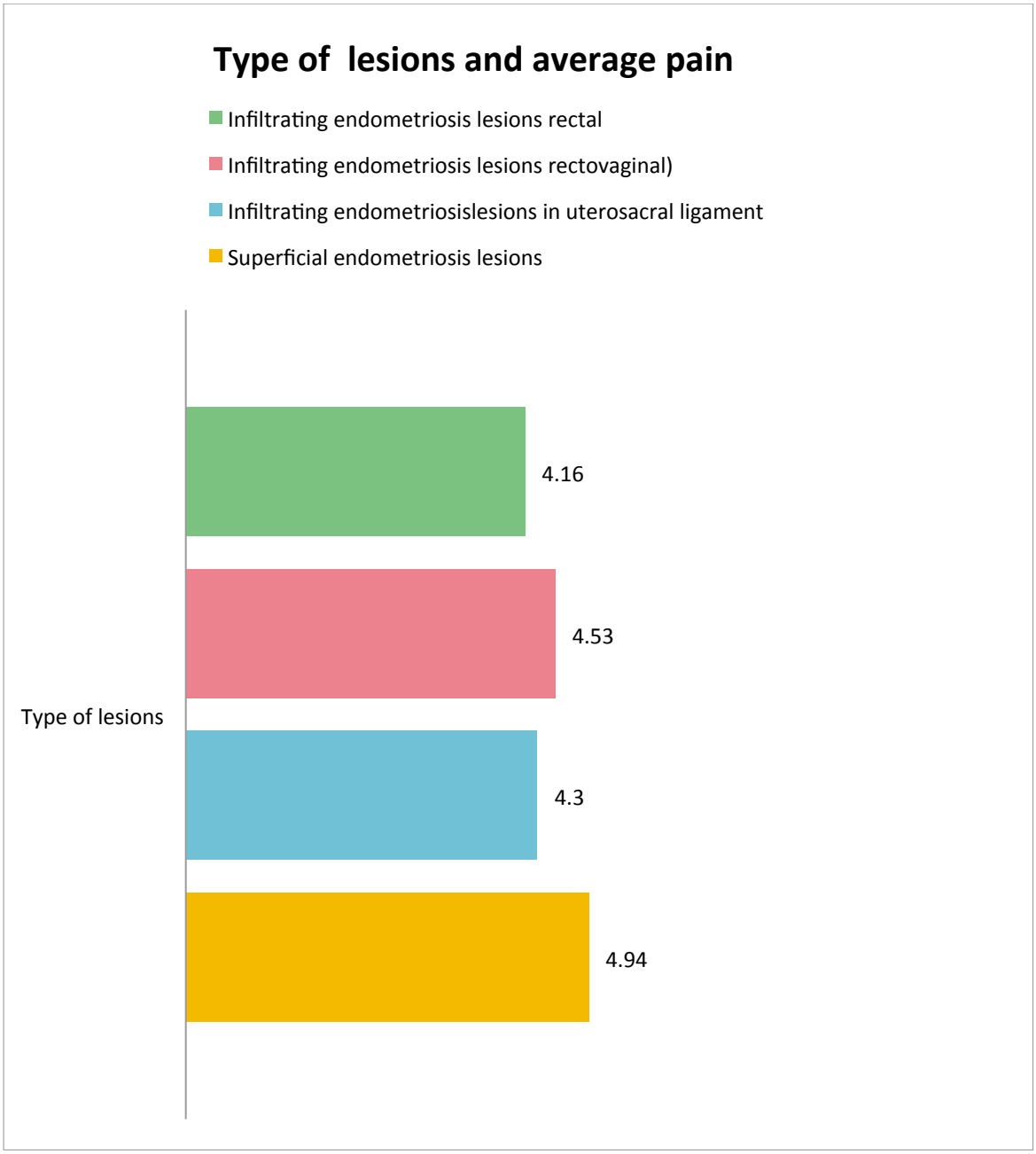

Fig. 31: Average pain in last month in superficial and infiltrating endometrial lesions (VAS scale from 0-10)

Psychiatric diseases and pain

There was a small positive correlation between the pain and the occurrence of psychiatric diseases, with $\rho = 0.1$, figure 32. No correlation between the development of psychiatric diseases and the origin of the pain (between endometriosis patients and patients with pain other origin) was found, with $\rho = 0.05$.

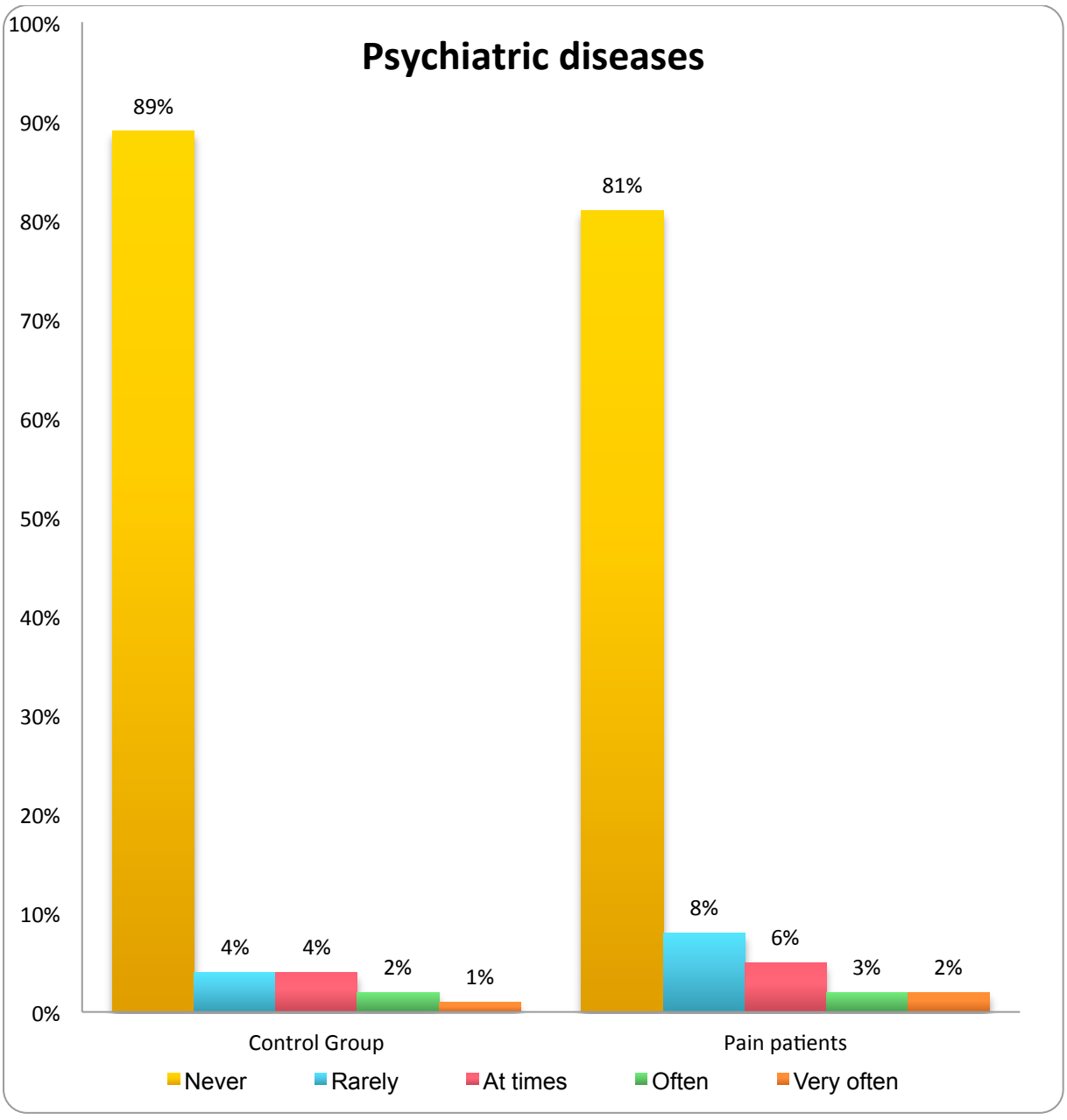

Fig. 32: Psychiatric diseases by endometriosis patients and control group (%)

Psychiatric treatment

There was a light positive correlation between pain and women who were under psychiatric treatment, with $\rho = 0.15$, figure 33. 29% of the pain group had been treated for a psychiatric disease in comparison to 13% of the control group.

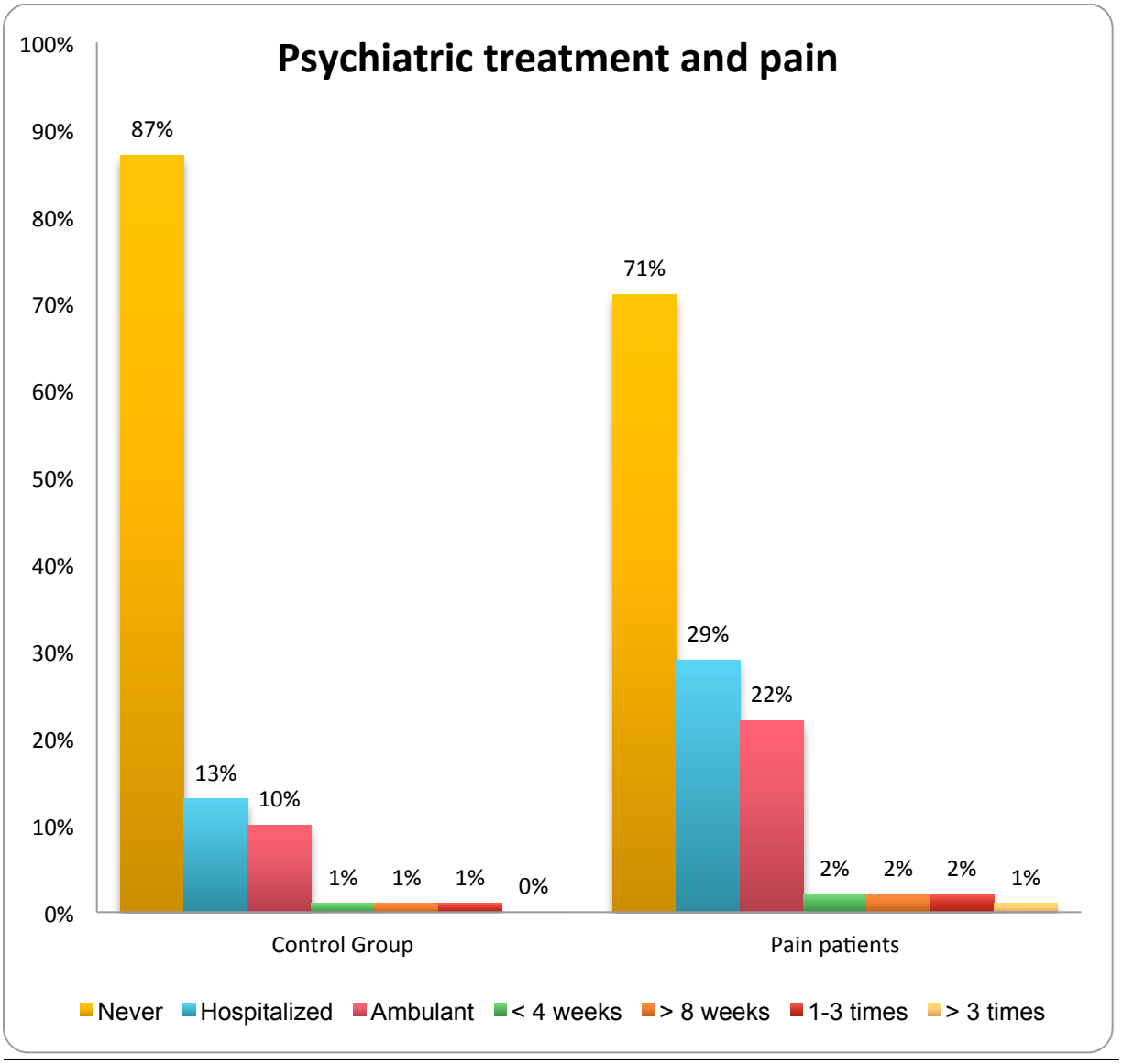

Fig. 33: Psychiatric treatment by endometriosis patients and control group (%)

The main reason for psychiatric hospitalizations (43%) in endometriosis pain patients was due to depression, summarized in figure 34. There was no correlation between the development of psychiatric diseases and the origin of the pain, ($\rho = 0.03$).

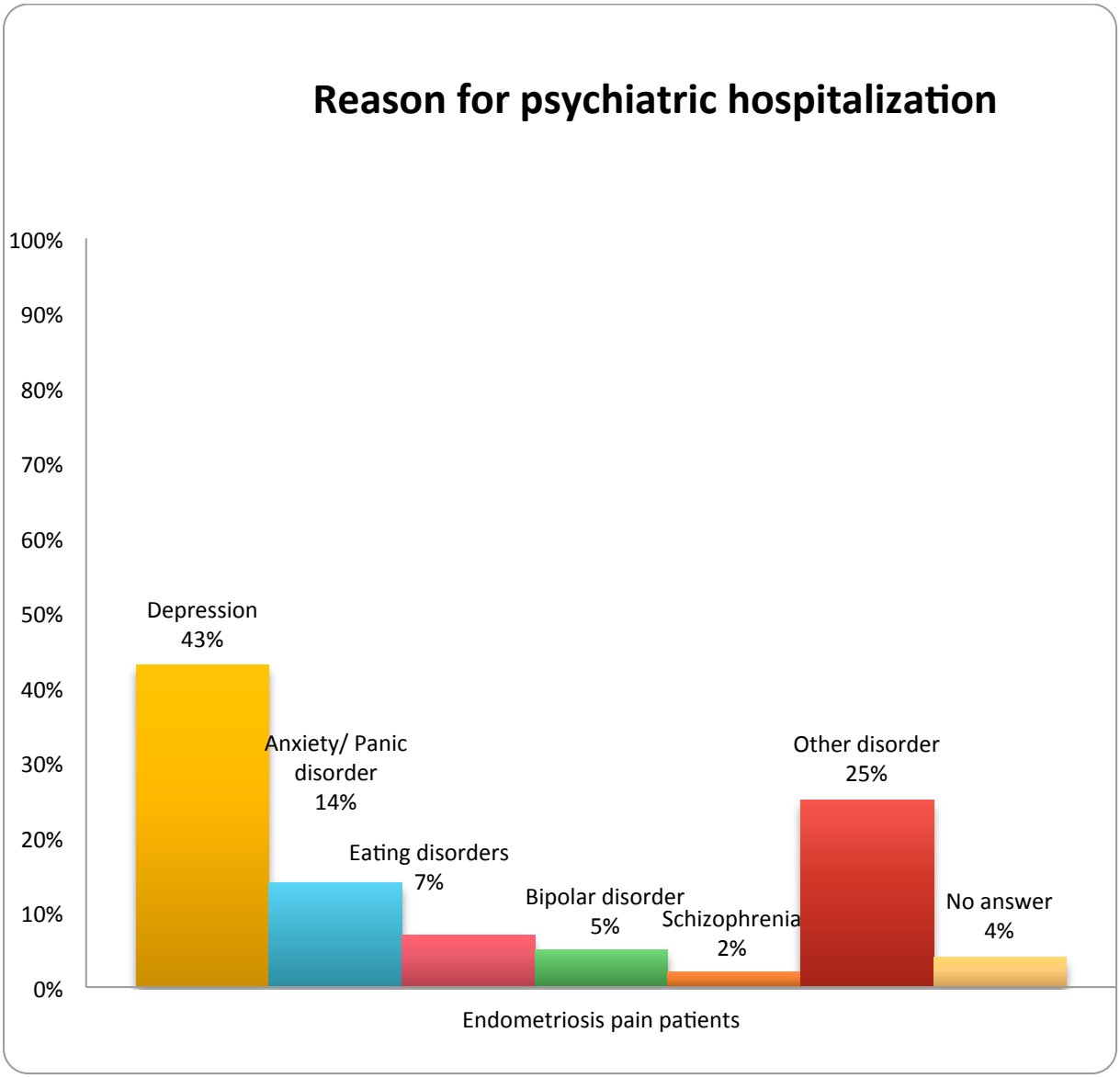

Fig. 34: Reason for hospitalization among endometriosis patients (%)

There was a positive correlation between pain, and women who had undergone psychotherapy ($\rho = 0.28$). 29% of the control group had psychotherapy in comparison to 57% of the pain group. 38% of the pain patients that decided for therapy did so because of endometriosis.

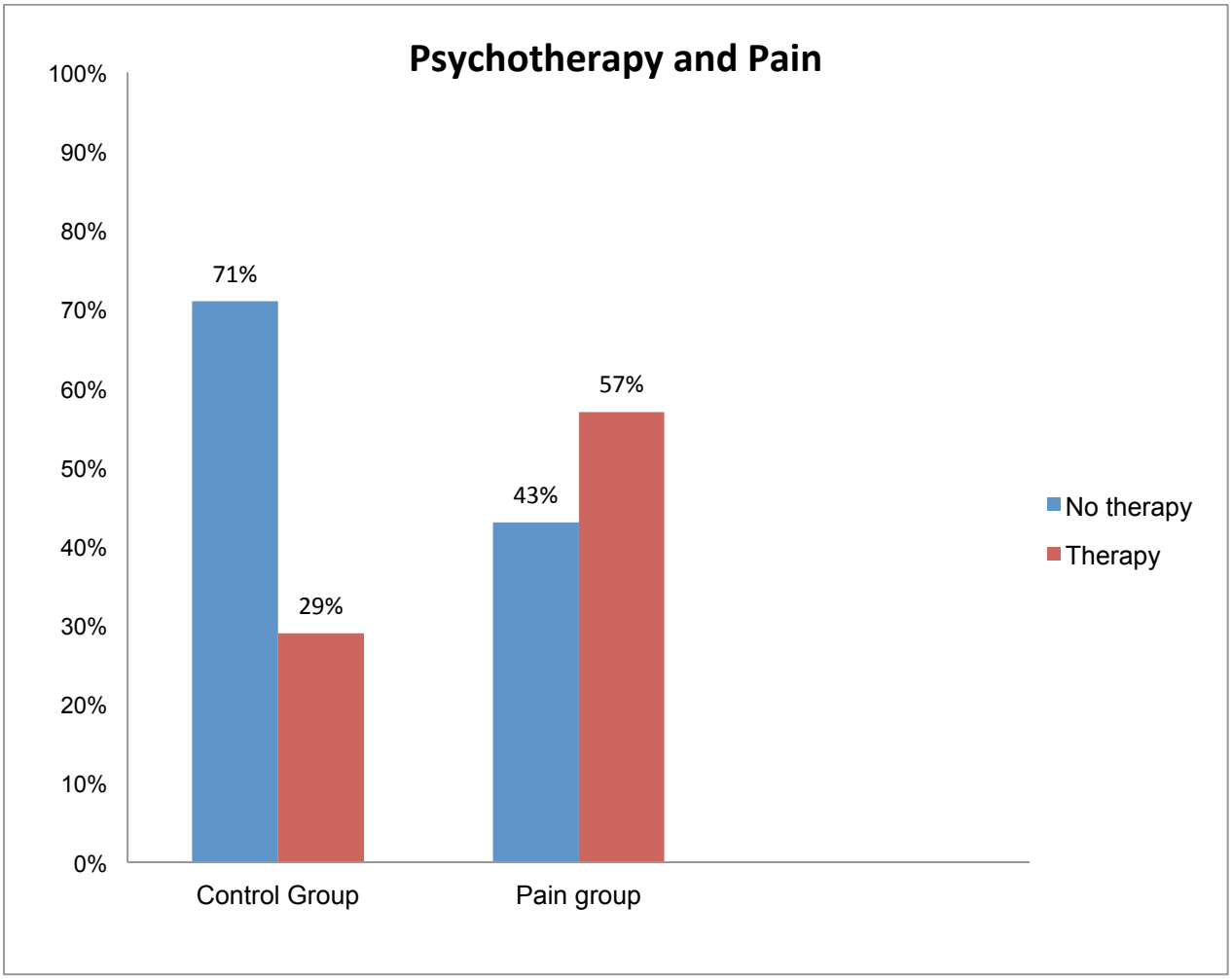

Fig. 35: Psychotherapy in pain patients and control group (%)

Depression

There was a high positive correlation between pain and depression with ρ = 0.46, (figure 36). 73% of the pain patients answered that they experienced depression at least once in their life, in comparison to 33% of the control group. A low positive correlation between depression and the origin of pain at ρ = 0.18 was also found. The endometriosis patients experienced depression more often than the participants with pain of other origin.

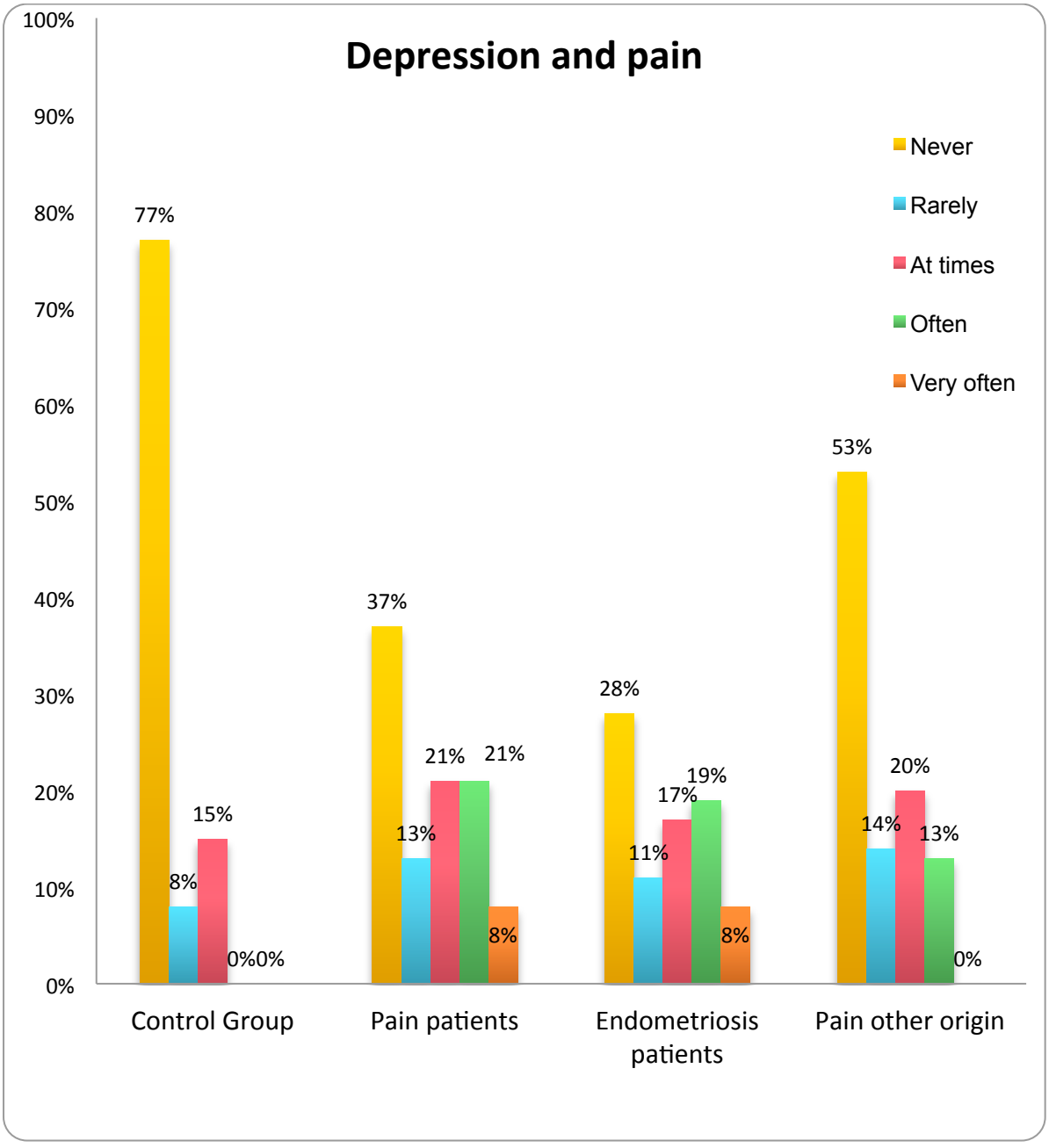

Fig. 36: Depression in pain patients and control group (%)

Evaluation of depression according to the PHQ-9 Score

The correlation between pain and the PHQ-9 Score is summarized in figure 37. The patients from the pain group scored higher in the questionnaire; pain patients had scores that indicate a mild depression, in comparison to normal scores from the control population, p-value < 0.0005

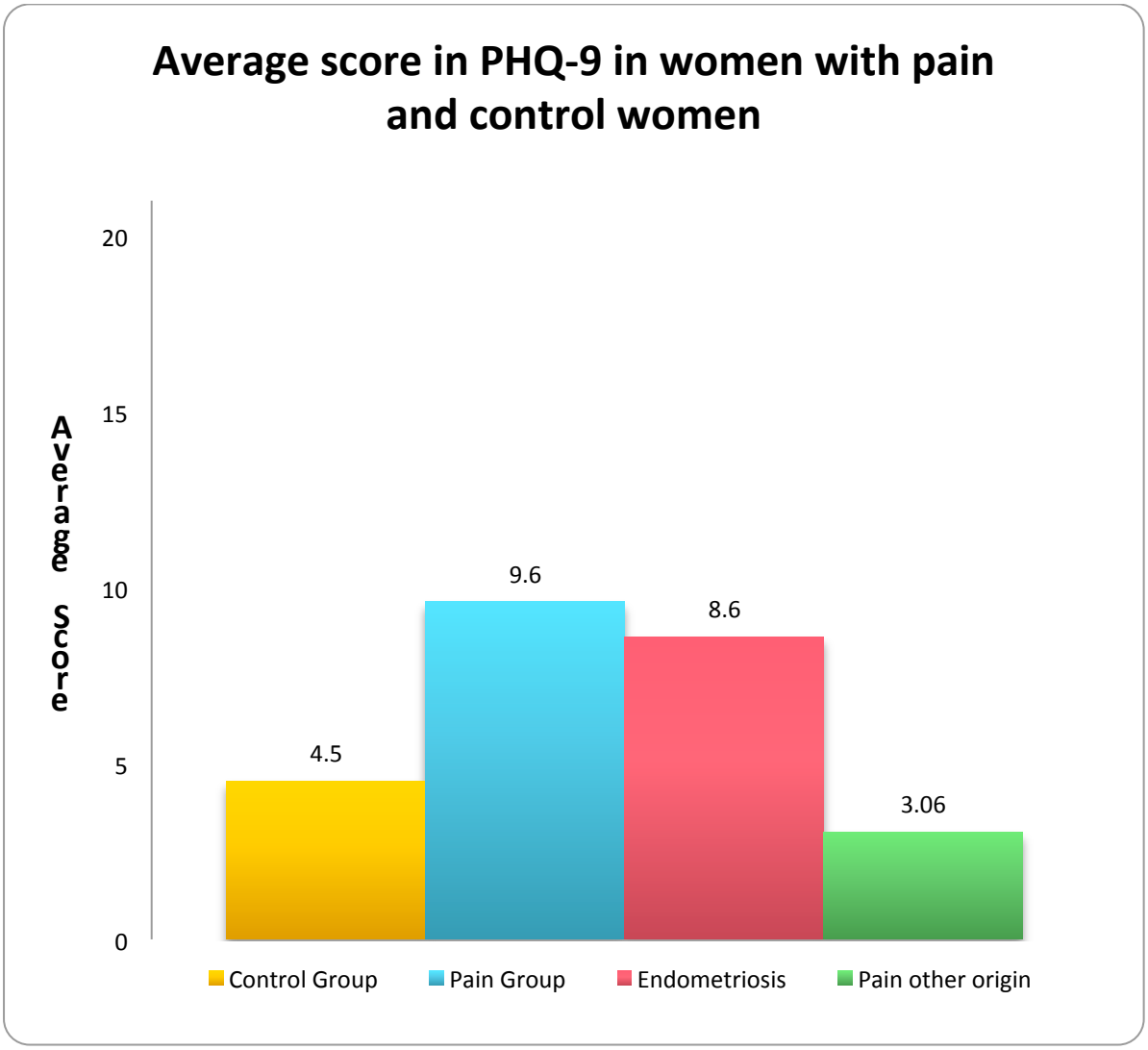

Fig. 37: Average PHQ-9 Score in pain patients and control group:

>5 mild depression, >10 moderate depression, >15 moderately severe depression,

>20 severe depression

Stress

There was a high positive correlation between pain and stress, with $\rho = 0.53$. The majority of pain patients felt stressed often or very often, in comparison to only 10% of the control group, figure 38, p-value < 0.0005.

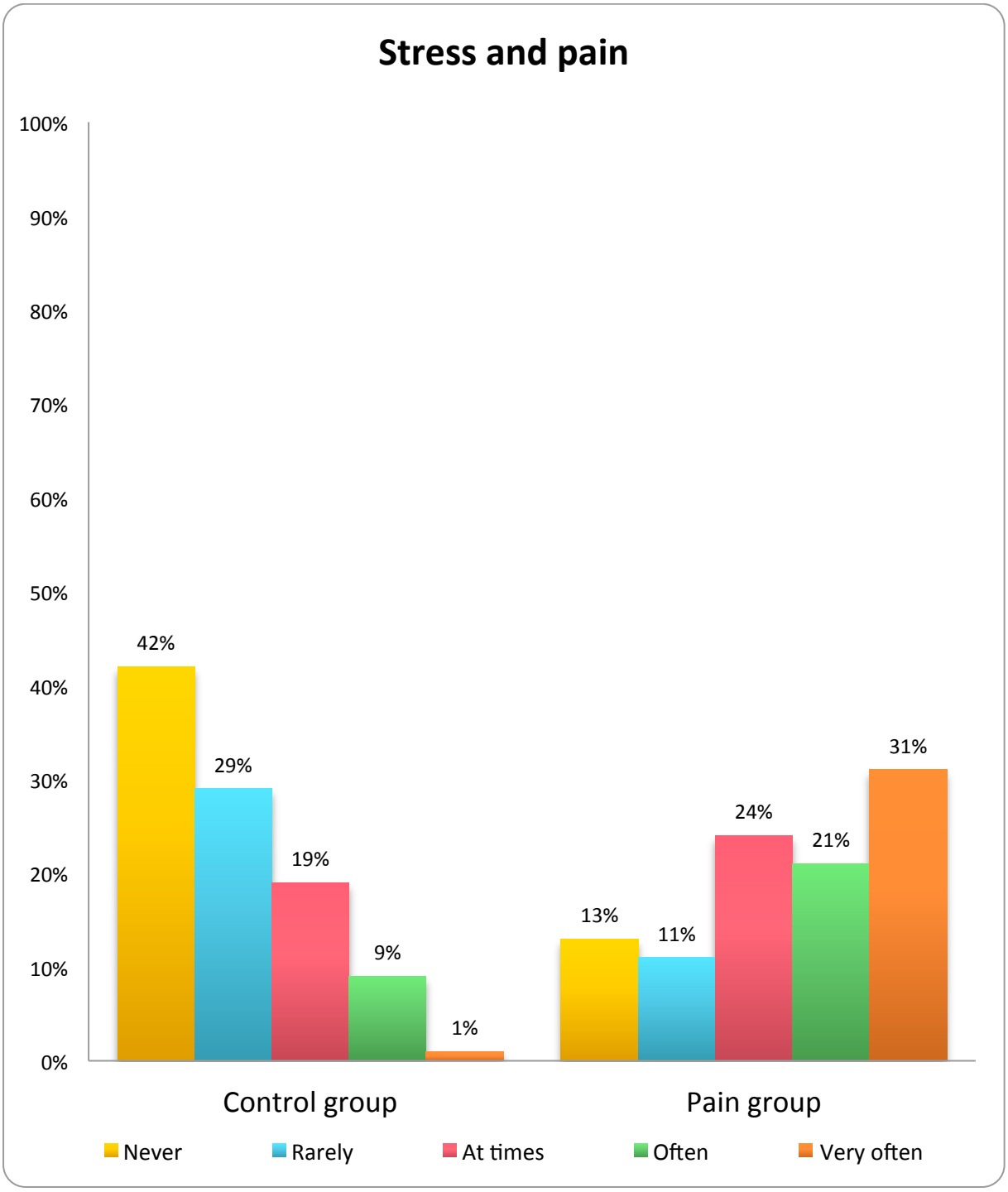

Fig. 38: Stress (in %) in pain patients and control group

Evaluation of stress according to the GAD-7

The correlations between pain and GAD-7 scores are summarized in figure 39. People with pain had more stress in comparison to the control group.

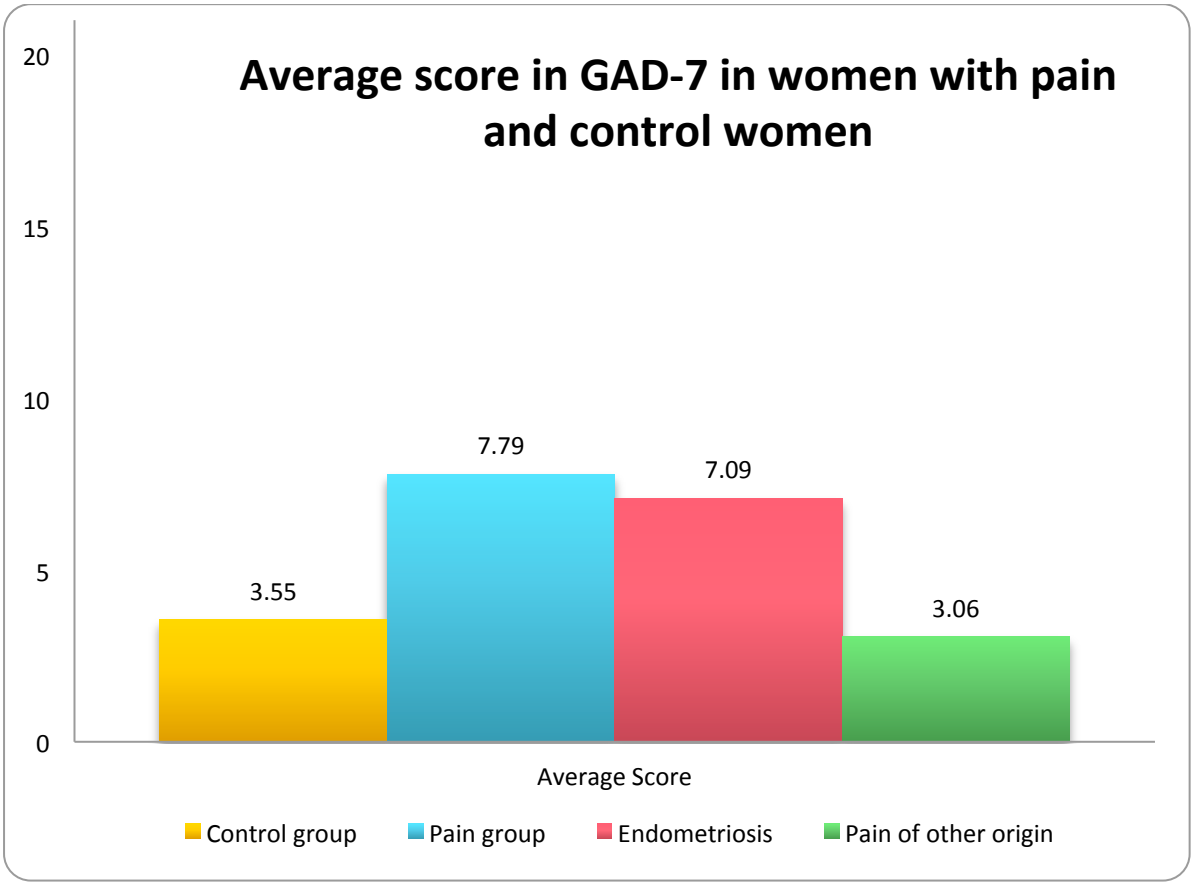

Fig. 39: Average GAD-7 Score in pain patients and control group. A score of > 10 indicates significant anxiety

Menarche and pain

Experience of menarche

In our study there was no correlation ($\rho = 0.08$) between the memory or acceptance of menarche between pain patients and the control group. Despite this, the majority of the pain group had either more unpleasant menstruation experience or definitely unpleasant menstruation experiences during their adolescence, figure 40.

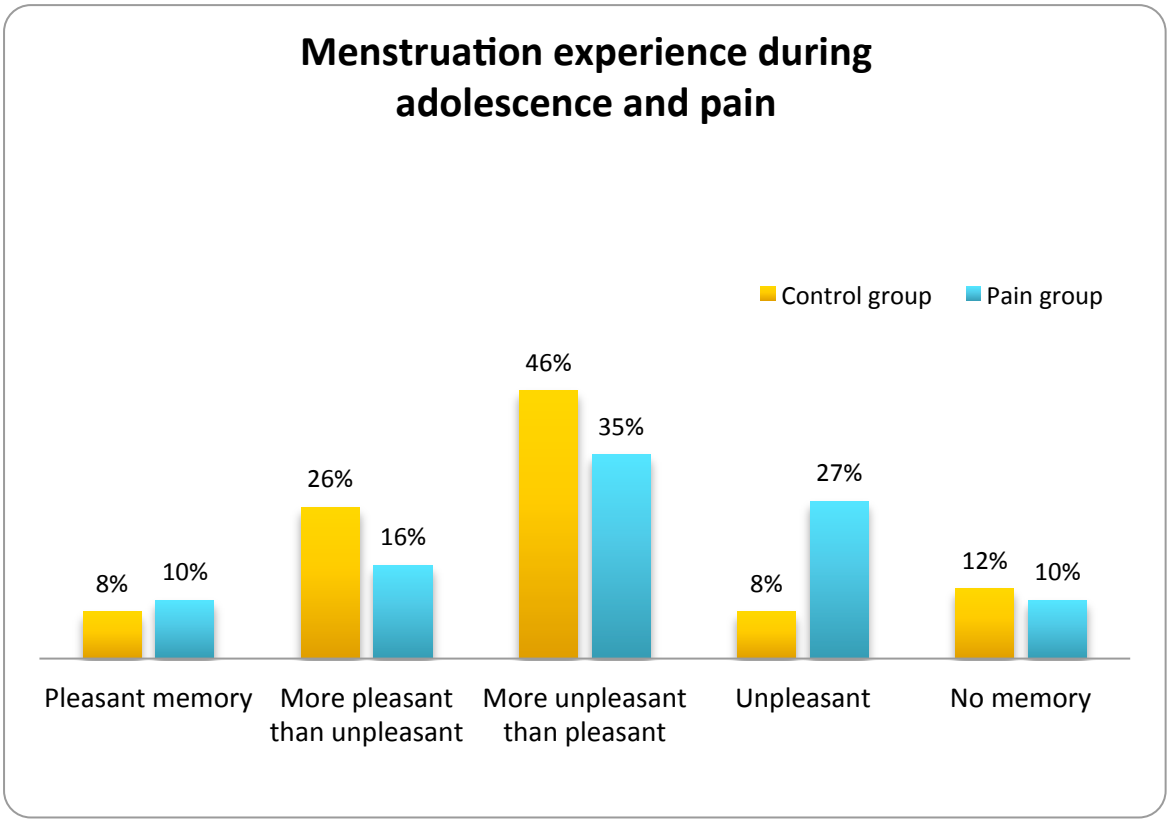

Fig. 40: Experience of menarche by pain patients and control group

Of the endometriosis patients, 79% had dysmenorrhea in comparison to 17% of the control group, figure 41. Of these women in the endometriosis group, 42% had primary dysmenorrhea. However, there was no correlation between primary dysmenorrhea and unpleasant memories of patients' first menstruation, with $\rho = 0{,}016$.

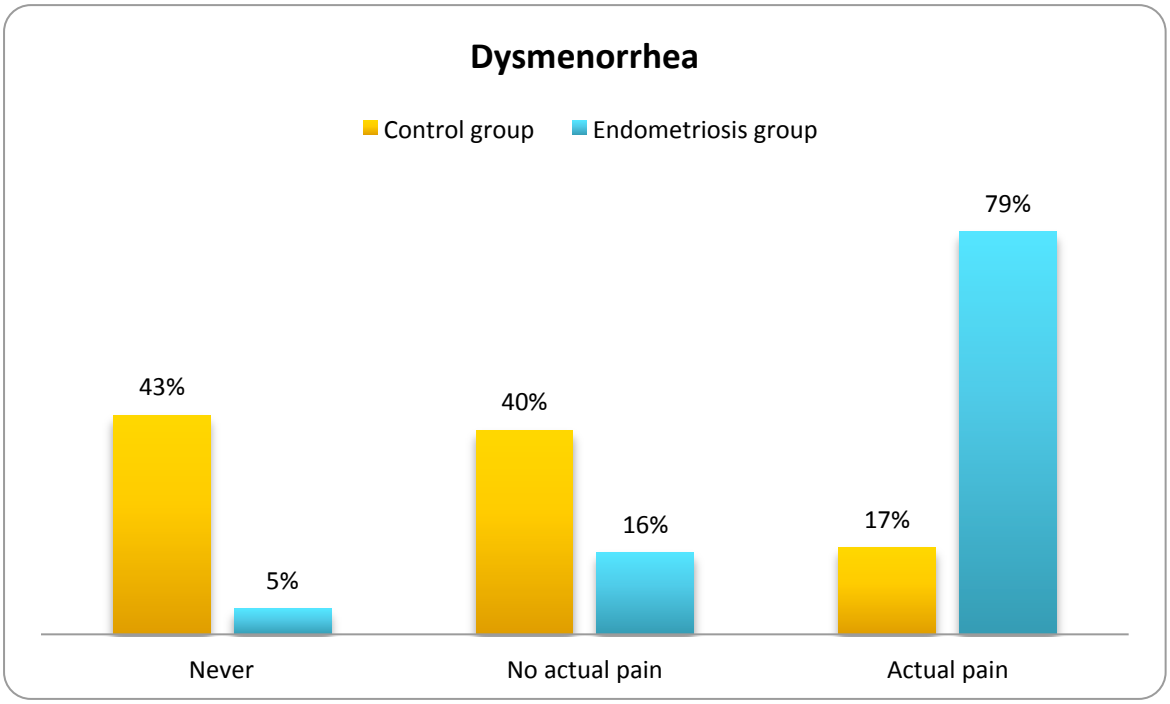

Fig. 41: Dysmenorrhea in endometriosis patients and control group (in %)

A correlation between a negative memory of the first menstrual period and the aggravation of chronic pain associated with endometriosis was found, ($\rho = 0.2$). Patients with a negative memory of their first period claimed a higher VAS score representing pain intensity (VAS=5.2, N=45) over the previous four weeks at the time of filling out the questionnaire in comparison with people of pain and a positive memory of their menstruation (VAS=4.6, N=23).

Maternal reaction to menarche and pain

In our study, no correlation between a positive reaction of the mother concerning patient's menstruation and pain was found with P = -0.05, (figure 42).

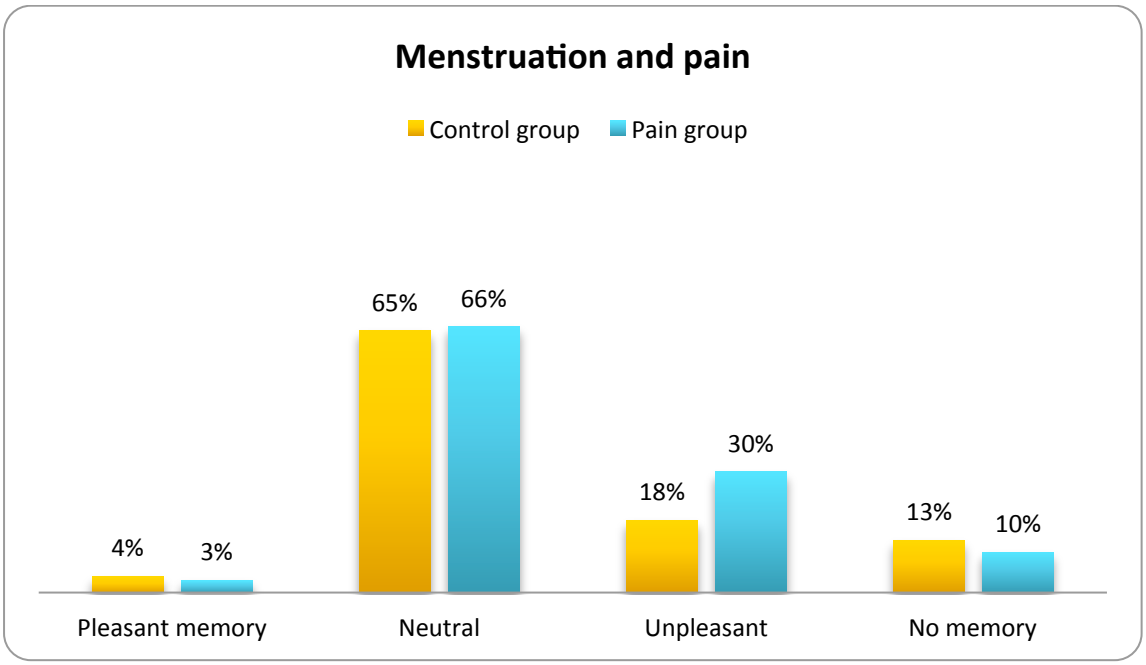

Fig. 42: Family's experience of menarche by pain patients and control group (%)

Experiences in childhood and pain

In our study we found initially no differences regarding childhood experiences between the control group and pain group. By examining experiences that indicate a difficult childhood we found no correlation between pain and those incidences; there was no difference regarding the experience of childhood abuse against the mother, drug abuse in the family, presence of a retarded family member, commit suicide in the family or family incarceration between the two groups. The Pearson coefficient was extremely low, at $\rho = 0.07$ (figure 43).

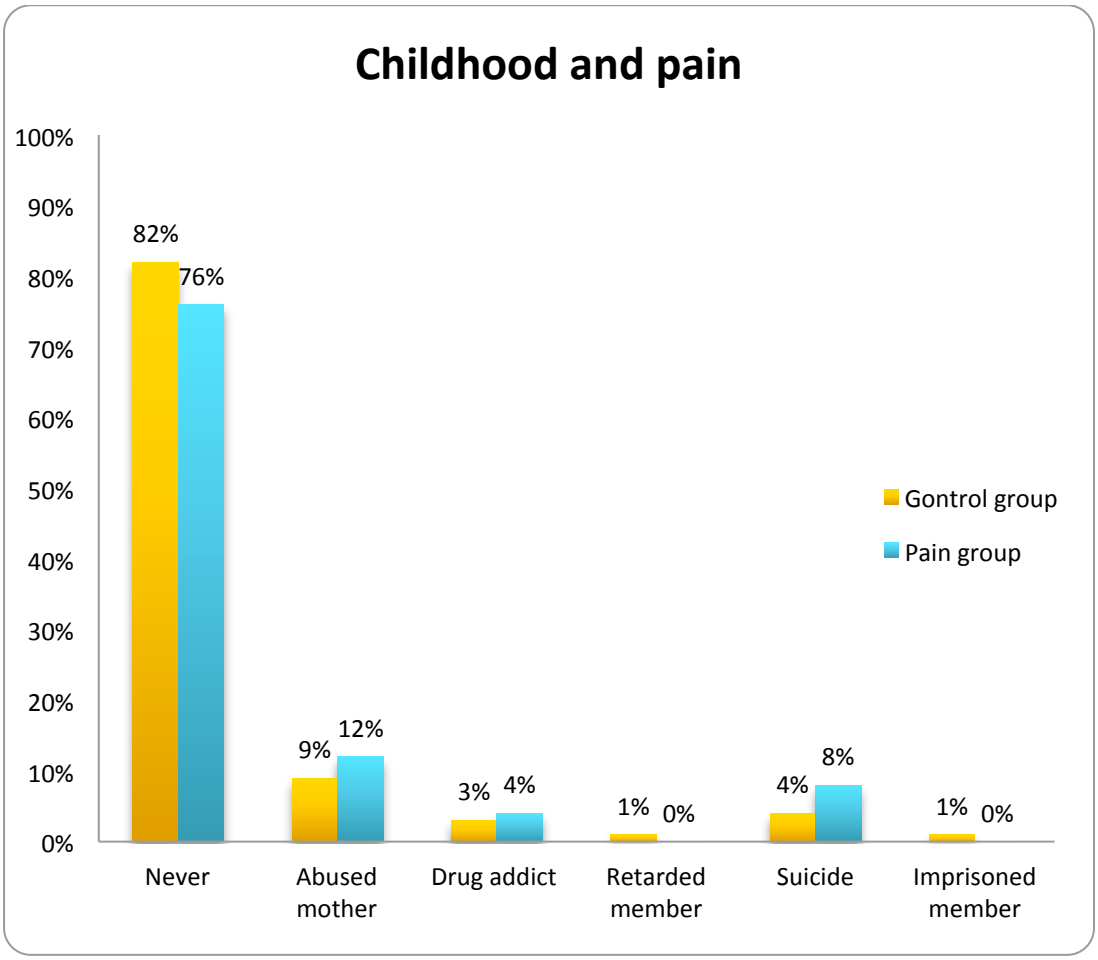

Fig. 43: Childhood experiences in pain patients and control group (%)

However, by going through more specific aspects of their childhood we did find a correlation indicating that people with pain did have more difficult childhood with higher incidence of physical abuse.

Physical abuse during childhood and pain

In the following figure, figure 44, we present the more specific differences regarding childhood experiences in the pain group and the control group.

We found a positive correlation between physical abuse during childhood and pain. The pain group had wounds marked by bruises from physical abuse ($\rho = 0.15$, p - value = 0.089) or they had been beaten with heavy objects ($\rho = 0.18$, p – value = 0.06) as well as they believed that they were more physically ($\rho = 0.13$, p – value = 0.01) and emotionally abused ($\rho = 0.23$, p – value = 0.34) during their childhood in comparison to the pain-free group.

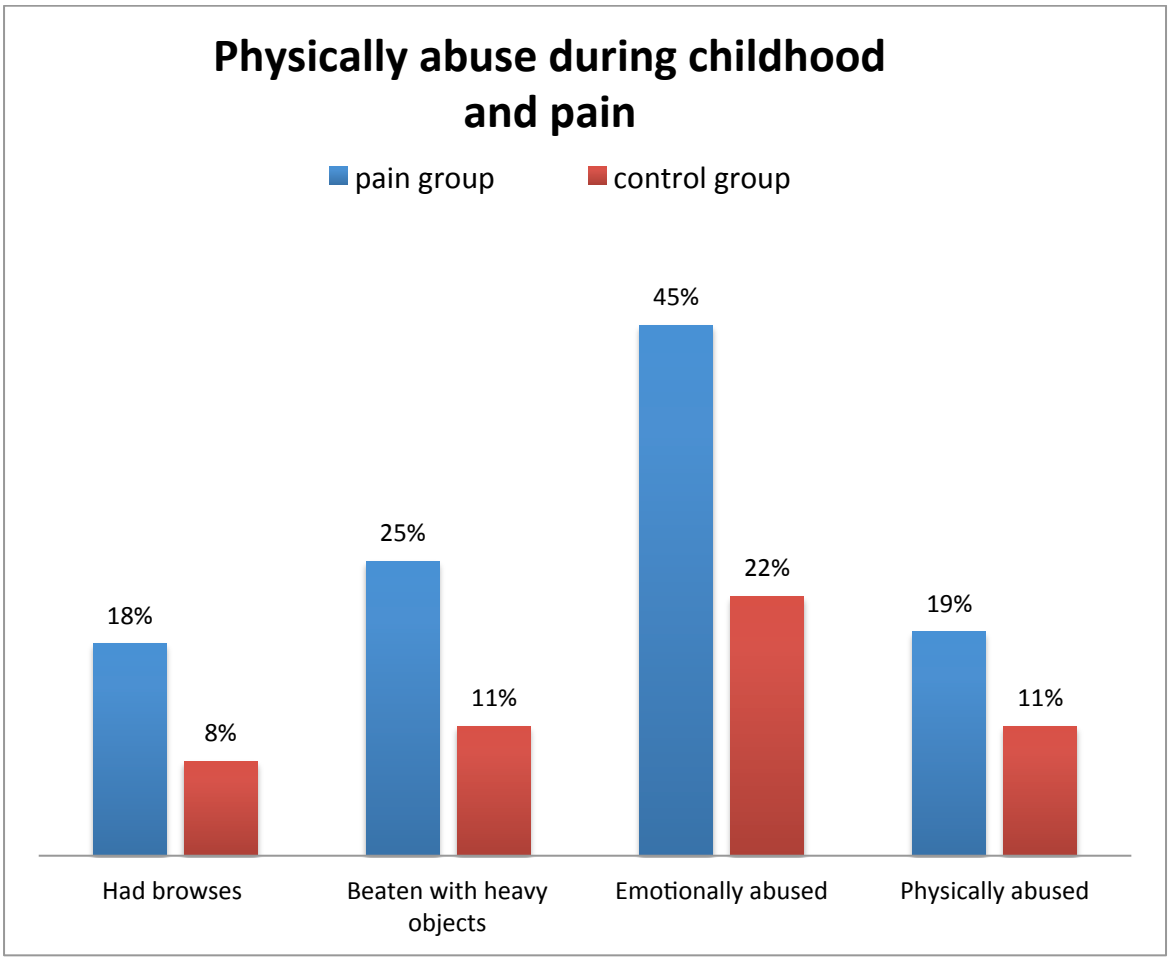

Fig. 44: Childhood experiences in pain patients and control group (%)

Sexual abuse and pain

There was no correlation between sexual abuse (ρ = 0.08, p – value = 0.25) and / or inappropriate touching during childhood (ρ = 0.06, p – value = 0.17) and later pain experiences. For sexual abuse that occurred later, during adolescence also no correlation with pain was found with ρ = 0.02, p –value = 0.17, figure 45.

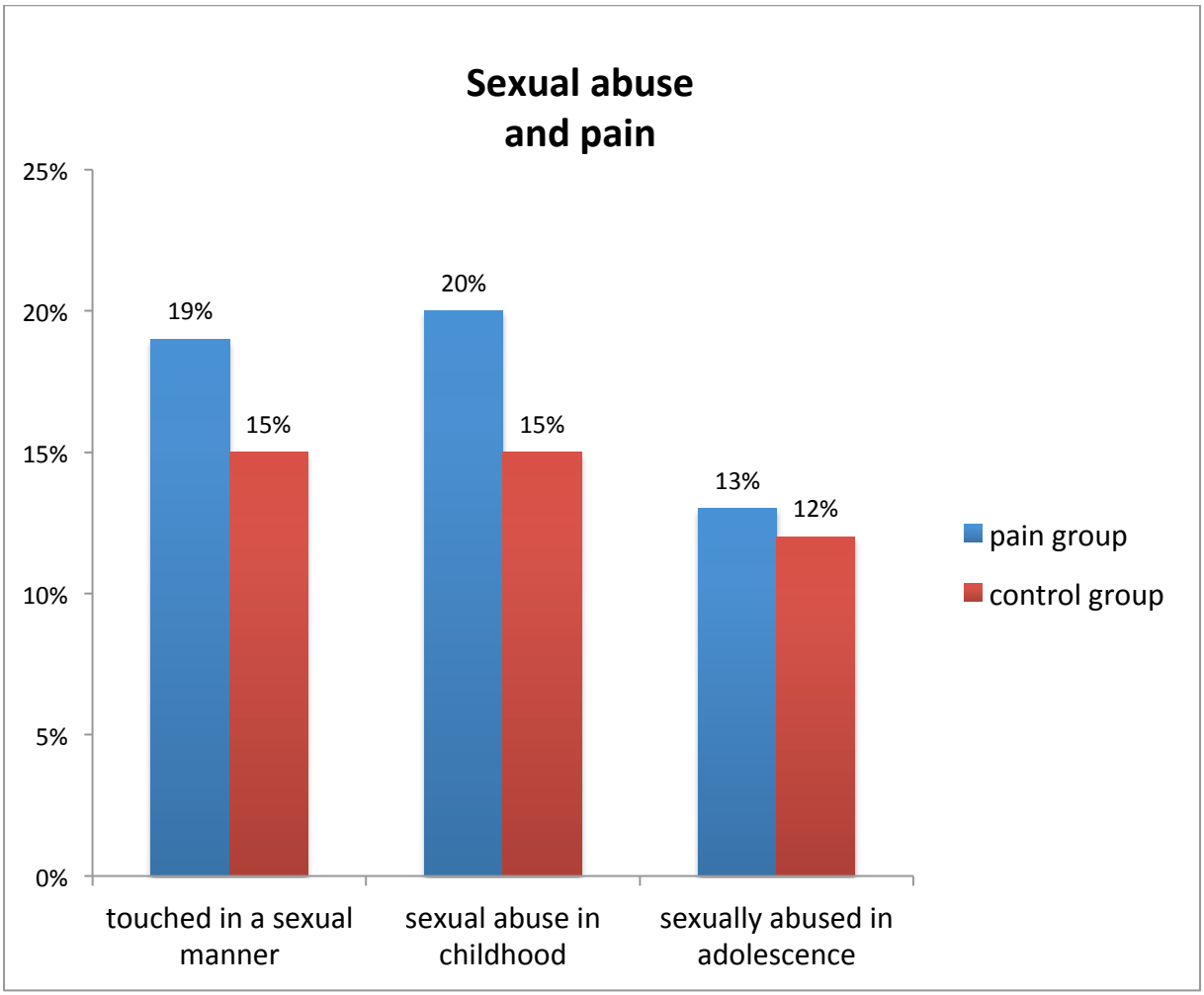

Fig. 45: Childhood experiences in pain patients and control group (%)

6. Discussion

Endometriosis is the most frequent cause of pelvic pain in women of reproductive age [25]. It may cause prolonged suffering and disability and can negatively affect health-related quality of life. Although CPP and severe dysmenorrhea are the most common symptoms of endometriosis, there are up to 30% patients with confirmed endometriosis that do not present any pain [33]. The absence of a correlation between the endometriosis severity, and the presence of pain, suggests a possible link between the psychosocial features of the affected women and her perception and regulation of pain [34].

According to the present results, endometriosis patients who suffer from chronic pain have higher prevalence of depression as well as anxiety. Furthermore, our results show that they have been hospitalized in psychiatric institutions more often than women from the general population, or women with chronic pain of other origin than endometriosis.

In our study we found in endometriosis patients with CPP, no correlation between the prevalence of pain and a history of sexual abuse or inappropriate touching during childhood or adolescence. However, a higher prevalence of physical and emotional abuse, both in childhood and in adult life did correlate with the presence and experience of pain. The non-endometriosis pain group showed no such correlation.

Furthermore, we found that a difficult acceptance of patient's menarche and the associated physiological body changes through adolescence is correlated with the aggravation of chronic pain associated with endometriosis. In our study we found that patients with a negative memory of their first menstruation, or whose mothers had a negative reaction to their first period develop more intense pain. Women who suffered from rejection from their family due to physiological body changes during menarche may be more sensitive to pain.

Additionally, we investigated the characteristics of the pain and the connection to endometriosis characteristics: in particular, to the stage, type and site of endometriosis. Like the majority of publications, we found no correlation between the stage of endometriosis and the intensity of pain as well as the duration and frequency of pain. In our results, the severity of pain due to endometriosis was significantly correlated with endometrial lesion size. Endometriosis patients with larger (>3cm) lesions presented more intense pain.

In the following section we will compare the most important results of our study with the current studies on psychosomatic aspects of endometriosis-related pain.

Demographic factors and pain

In our study, in order to investigate whether endometriosis patients with chronic pain share specific personal characteristics in comparison to the general population, as well as other pain populations, the selection of the sample was made very carefully. The control and endometriosis patient groups were matched according to age, nationality and education status in order to minimize the differences between the two groups, and arrive at a suitable comparison of their personality characteristics.

No significant difference in the civil statuses between endometriosis group and control group was found; the majority of endometriosis group were in a relationship (81.7%) in comparison to 80.7% of the control group. A difference in the civil statuses might have been expected given the impact that symptoms of endometriosis can have in the relationship. Other studies have shown that the continuous presence of pain may disturb established or future affectionate relationships [20, 35, 36]. Our data showed no indication of this.

This however could be explained by the fact that a partner can be a great source of support for many women suffering from chronic disease. In cases of severe pain, partners can take over duties and be a great emotional and practical support [11]. This explanation might be the reason for the high rates of a being in a long-term relationship in the pain-due-to-endometriosis group. According to our results, all patients with endometriosis who were experiencing pain were in a relationship, in comparison to 80% of patients with pain of a different origin. There was also a small correlation between pain and being in a long-term relationship. Of course not all partners are able to stand the constant burden of coping with a chronic disease, which can result in an increased separation rate and marriage breakdown, as shown in [37]. However, this might be an oversimplification as it is difficult to specify the causes leading to a marriage breakdown.

Despite of most of the patients being in a relationship, and the majority of pain patients had no children (68%, in comparison to 52% of the control group). The percentage was even higher in pain patients due to endometriosis, at 75%. It is well established that infertility is one of the main symptoms in endometriosis patients. In women with endometriosis, the frequency of infertility is estimated to lie real up to 30% and 40%, with the risk of infertility 20 times greater than in women without endometriosis [38, 39]. In our study, as would have been expected, there was a high negative correlation between endometriosis and maternity

with $\rho = -0.34$. The anti-correlation was even higher between pain-due-to-endometriosis patients and maternity. It is however not clear whether this high anti-correlation had to do with patients' decisions not to have children or whether it is directly due to infertility. The majority of the study participants had difficulties to conceive: almost 65% of those who had difficulties to were endometriosis patients, 2.5 times more frequent than patients with pain from a different origin. We must mention that for the set of questions regarding difficulties to get pregnant, few women answered, only 150 out of the 208 participants, despite the questionnaire's anonymity.

Studies point to the age at which woman first gave birth as the main factor contributing to menstrual pain - it is hypothesized that an earlier start to reproductive life decreases the sensitivity of the uterus to prostaglandins [40]. Unfortunately the questionnaire did not ask for the mother's age at the time of the first birth, so we are unable to address such correlations in this study.

No significant difference between sports and nutritional habits, smoking and drug habits, as well as professional life between pain group and control group was found. It was hoped that the investigation of the link between different life style factors and the experience of pain could lead us to conclusions that point out the importance of those factors in the genesis and experience of endometriosis-associated chronic pain. Accordingly, this could aid in the recommendation of treatments, in which specific life style model could be integrated into new therapeutic options. Our data showed no such connections.

Characteristics of endometriosis according to the operative reports

Stage

Almost half of our endometriosis patients were in stage IV (44%). 14% were in stage I, 13% in stage II, and 29% in stage III. The reason for the inhomogeneous sample and the high number of patient in stage IV could be because our endometriosis group mainly consisted of self-help groups (64%). These members have coped with the disease for years, and have undergone operative treatment because of symptoms such as pain or infertility. 56% of our endometriosis group had been through a laparoscopy at least twice in their lives. Also, endometriosis patients in stage I usually experience accidental diagnosis [41]. Ferrero at al [42] found also that the majority (86.8%) of women who had been through laparoscopy were in stage III and IV.

The correlation between pain intensity and the stage of the disease has been well examined. Previous studies indicate that the endometriosis stage was not related consistently to pain symptoms [13, 27] and agree that there is no correlation between the stage of the disease and the intensity of pain, concluding that the current classification system (See rASRM, table 1) correlates only with endometriosis-associated dysmenorrhea [31, 32, 43, 44, 45, 46, 47]. In our study, we also found no correlation between the stage of endometriosis and the intensity of pain ($\rho = 0.02$) as well as the pain characteristics such as duration and frequency. It's possible that this correlation (or in this case, the lack thereof) is dependent on endometriosis classification scheme according to rASRM itself. Possibly, the rASRM classification is not detailed enough. For example the presence of lesions in the uterosacral ligament and the involvement of intestines are parameters that are not considered in the rASRM classification despite many studies that show that they can influence the severity of pain [43, 44, 45].

Location

In our study no correlation was found between the intensity of pain and the location of endometriosis lesions. The average pain didn't differ between the anatomical places as they have been correlated in other publications with aggravation of pelvic pain or dysmenorrhea. Previous studies indicate that the severity of pain due to endometriosis is significantly correlated with the location of endometriosis lesions, with particular reference to deep infiltrating endometrial lesions [17, 31, 43, 44, 45, 46, 48]. Deep dyspareunia was associated frequently with the presence of vaginal lesions [31], while ovarian endometriomas are lesions

significant associated with severe dysmenorrhea and pelvic pain [32]. Some studies suggest a strong correlation between the frequency and intensity of chronic pain, and the presence of lesions in the uterosacral ligament [43, 44, 45]. Stovall et al. [46] showed that the uterosacral ligament involvement was related to a high severity of chronic pelvic pain and deep dyspareunia. Furthermore, that an intestinal involvement was related to an increased severity of dysmenorrhea and gastro-intestinal symptoms, while another study [45] showed that the frequency of noncyclic chronic pelvic pain was higher when it involved the bowel. The reason for our different results could be the currently still-limited number of our sample; note that only 64 women of the endometriosis group answered the following questions. A more representative number of women with endometriosis with lesions in different anatomical areas will result in more representative results.

Adhesions

Based on the existing literature, other factors that can influence the intensity of pain are the presence and the extension of pelvic adhesions. Many studies show that there is a positive correlation between the type, the degree, and the location of the adhesions, especially those in the pelvis and on the adnexa, and the severity of pain [31, 43, 45, 47, 49]. Strathy et al. [43] documented that adhesions of the bottom and posterior wall of uterus were positively correlated with dysmenorrhea and chronic pelvic pain, while adhesions of fallopian tubes were positively correlated with dysmenorrhea, chronic pelvic pain and dyschezia. Adhesions of the rectum were positively correlated with dysmenorrhea. Also, the frequency of severe dysmenorrhea increased with Douglas pouch adhesions [45]. The extension of the adhesions also defined as a critical factor that interferes with the intensity of the pain. In [44], the authors concluded that the severity of CPP significantly correlates with the extent of peritoneal and adnexal adhesions. In our study we confirmed that there is indeed a positive but small correlation between pain intensity and the existence of adhesions (P=0.20), but no correlation was found between pain intensity and the location of endometriosis adhesions. Furthermore, there was only a trend between intensity of pain and the type of adhesion: dense adhesions are associated with more intense pain ($\rho = 0.15$). The reason for this difference could again be the limited number of our sample.

Type and number of endometriotic lesions

The severity of pelvic pain and dysmenorrhea has also been correlated with the total number of superficial implants and with the lesion types. Deep infiltrating endometriosis, in contrast to superficial endometriosis, is known to cause intense pain-related symptoms depending on the anatomical region and infiltration depth [50, 51]. Other studies [17, 44] contradicted these results and found no correlation between the pain score and the partial score of superficial endometriosis, the total number of endometriosis implants, the number of typical implants and the number of atypical implants. In our study neither the number nor the depth of the endometrial lesions were correlated with the intensity of pain.

However, there was a low correlation between the intensity of the pain and the size of the endometrial lesions (P=0.142). Patients with bigger lesions (>3cm) presented more intense pain. This result partly supports studies suggesting that endometriosis-associated pain is due to the lesions. A new study [50] suggests that endometrial lesions can develop their own nerve supply, creating a direct and two-way interaction between lesions and the central nervous system. This provides a mechanism by which the nervous system is brought directly into play to produce a variety of individual differences in pain that can, in some women, become independent of the disease itself [50].

Endometriosis specific characteristics of pain

In our study pain was very frequent among endometriosis patients. 77% of the endometriosis patients experienced pain at least once a week. In the literature, among women who undergo laparoscopy because of CPP, 40% to 60% are found to have endometriosis at the time of the laparoscopy [1, 2, 13, 52]. Our higher prevalence of pain might be due to the composition of our endometriosis group, consisting 64% of self-help group patients, including women who had been operated at least twice because of pain.

In 56% of the pain-due-to-endometriosis cases, the pain was not related to the menstruation, as was expected from the literature [13, 47, 52]. The average duration of pain was 4-9h per day and didn't differ between the endometriosis group and the non-endometriosis pain group.

In our study, endometriosis patients had pain for a longer portion of their lives than patients with chronic pain of a different origin. The majority, 76%, of endometriosis patients had pain at least for the five past years in comparison to 54% of participants with pain of a different origin. This agrees with the existing literature in which the average time between first symptoms and diagnosis of endometriosis is between 6 to 11 years [10, 53].

The intensity of pain was evaluated by using a 10-point visual analog scale. The average pain scores, the average maximum pain and the average pain that the patients were experiencing at the moment of the study, didn't differ between the patients with pain due to endometriosis and the pain group of pain of another origin. The majority of the patients with pain of other origin than endometriosis were suffering from back pain or headaches. The fact that the patients in both pain populations presented the same intensity of pain regardless the localization of pain or the stage of the disease indicates that the pain burden is due to factors other than localization or example the frequency of the pain. Another explanation is the fact that a sample of patients with pain will score close-to-uniformly over the range from 1 to 10, excluding zero as in this case they would be excluded from the study. The mean of this distribution is approximately 5, implying that the average of any pain population score will be close to this value, as was found in our study for both pain groups.

The fact though that the patients in both pain populations presented the same intensity of pain enabled us to investigate the psychological status of the participants independent of the severity pain. Intense pain is associated with despair, resignation and depressive moods [11],

and complicates the investigation of whether psychological factors, prior to the chronic endometriosis-associated pain, could be important elements of pain genesis pain perception.

Despite the participants of the two groups not having presented any difference regarding the intensity of the pain, the disruption of daily life due to pain among endometriosis patients was higher than for patients with pain of a different origin. Patients with endometriosis presented dyschesia, dysuria and dyspareunia. Among endometriosis patients with pain, there was a greater loss of social activities than among non-endometriosis pain patients. In our study, endometriosis patients scored much higher in the pain disability index in comparison to the pain group from another origin. Endometriosis patients' pain influenced their social activities (an average score of 5.54 in pain disability index in comparison to 2.46 in pain group other origin). Endometriosis patients have to deal daily with disease symptoms such as pain and fatigue, which results in a reduced quality of life. We should not ignore the fact that the recurrence rate of endometriosis is extremely high: estimated at 21.5% at 2 years and 40–50% at 5 years [4]. As the recurrence risk of endometriosis is high, fear of relapsing represents an additional burden that may contribute to social isolation. While the social environment often provides support, women with endometriosis might prefer to hide their symptoms as they are scared that are not taken seriously, or because they detest being pitied [11]. Such feelings may interfere with everyday life, partnership and social activity. Another reason for the bigger disruption of daily life due to pain among endometriosis patients in comparison to patients with pain of a different origin could be the longer duration of pain among endometriosis patients. Endometriosis patients had pain for a longer portion of their lives than patients with chronic pain of a different origin. This fact can lead to a reduced quality of life.

In our study, endometriosis patients with pain scored higher in comparison to pain patient group of other origin in the pain disability index concerning sexuality. The endometriosis patient group gave an average score of 7.18 in comparison to 4.64 of the pain group of other origin. The high influence of endometriosis pain patient group on their sexuality must probably be related to dyspareunia that is also perceived as one of the main burden associated with endometriosis [8]. The majority of women with pain of other origin than endometriosis had back pain or headaches, which are not related to dyspareunia. Endometriosis patients, who often suffer also from dyspareunia, scored higher in comparison to pain patient group of other origin in the pain disability index concerning sexuality, as expected.
In addition, often endometriosis is associated with a negative female body perception and is known to affect the woman's confidence in her own body [11] which can also be responsible for the greater impact on their sexuality in comparison to women with pain of other origin.

Reasons other than the intensity of pain influence the impact of the disease as well as pain perception in endometriosis patients. Preveler et al. [48] suggested that women with endometriosis had somewhat more severe pain and greater social dysfunction than those with unexplained pain. Furthermore, several results from human as well as animal research emphasize the hypothesis that a generalized hyper-sensibility is involved in endometriosis related pain [11].

Psychosomatic factors

Psychiatric diseases: Depression and anxiety

According to the present results, endometriosis patients who suffer from chronic pain have higher prevalence of depression as well as anxiety. Furthermore, our results show that they have been hospitalized in psychiatric institutions more often than women from the general population, or women with chronic pain other origin than endometriosis.

Our study agrees with the results of previous studies that found that people with depression and other mental disorders seem to develop chronic pain and disability more often [54, 55]. Previous studies raised the question of whether depression and psychosomatic strain play a role in the etiopathology of endometriosis [40, 49, 56], but it seems more likely that such correlations are due to a consequence rather than a cause of the disease. Previous studies showed that women who suffer from CPP exhibit more evidence of neurotic behavior and a higher prevalence of depression, as well as social problems [2, 35, 57, 58]. Research into other chronic pain syndromes suggests that certain personality traits and coping strategies, including a tendency to “catastrophize”, may predispose an individual to the development of chronic pain and disability [31].

We investigated whether or not women with endometriosis-associated pain have more anxiety and more psychological stressors through the General Anxiety Disorder-7 questionnaire (GAD-7) and the Prime Health Questionnaire (PHQ-9) about Depression Severity. In our study, we found a correlation between depression and pain, as well as between anxiety and pain. Our results agree with previous studies that show that people with a neurotic personality and mental disorders develop chronic pain and disability more often [2,

24, 59]. More specifically: we indeed found a correlation between pain and PHQ-9 and GAD-7 scores. People with pain had more stress, and scored higher in both questionnaires. Pain patients had scores that indicate mild depression, in comparison to normal scores from the control population. By using our own formulated questions we found a high positive correlation between pain and depression (figure 37). There was a low positive correlation between depression and pain from endometriosis (P = 0.18). The majority of endometriosis patients with pain answered that they experienced depression at least once in their life (82%); in comparison to 47% of patients with pain different than endometriosis origin. This positive correlation between depression and endometriosis-associated pain makes one assume that this has to do with the severity of pain or the frequency of the pain. However, by examining the two groups, we saw that the two subgroups show no significant difference in the severity of the pain. There was a high positive correlation between pain and stress. 31% of the pain group felt stressed very often, in comparison to 1% of the control group.

Our results agree with previous studies that have shown that women who suffer from CPP present more evidence of neurotic behavior, and high rates of psychopathology and distress [2, 31, 59]. The question that arises is whether depression and stress are characteristics more common among women with endometriosis-associated pain as part of their character, or rather as a consequence of chronic pain. The latter hypothesis is supported by Sternbach et al. [60], who demonstrated that abnormal scores on standardized psychiatric instruments returned to near normal for chronic pain patients who had been cured of their pain. The existing studies have produced results that are inconsistent and contradictory [2,60]. Despite early reports of high rates of psychiatric morbidity, these studies suffer from a number of methodological weaknesses. The small sample sizes, and the comparison of groups were unmatched, calling these results into question. And most importantly, many reports lack accurate differentiation between causes and effects. On the whole, previous studies investigating psychopathology in CPP have failed to consider the fact that the reported psychopathology and distress in pain groups may be a possible long-term consequence of the experience of chronic pain, as opposed to a specific association with CPP.

In our study we found important differences regarding specific personality characteristics in women with chronic pain due to endometriosis than in pain group other origin, even though the pain characteristics were similar. This in our opinion suggests that personal characteristics of the endometriosis pain group are primary due to the pain symptoms, and that they may play an individual role in the development and the perception of endometriosis-associated pain. This is why the application of new medical models, focused on the psychosocial aspects

of the endometriosis is essential. On this background psychotherapy, pain-group attendance, and changes in lifestyle may help endometriosis patients to improve the quality of day-to-day life by reducing pain.

Experiences of menarche

Many studies showed that a difficult acceptance of patient's menstruation and of the physical changes through adolescence is higher among pain patients [2, 58, 61, 62]. The influence of the role of dysfunctional families in the experience of CPP was first mentioned in the literature by Duncan et al. [63]. Based on their study, women from families in which maternal warmth was typically lacking had a higher CPP prevalence.

In our study there was no correlation between the memory and the acceptance of menarche and pain between the two groups; nor between a negative reaction of the mother concerning patient's menstruation and pain (ρ 0.08). Despite this, 27% of the pain group has negative memories of their first menstruation, in comparison to 8% of the pain free group. We assumed initially that the reason for the negative menarche memories could be because of the presence of dysmenorrhea among those participants. As dysmenorrhea represents a common symptom of endometriosis [13] this could be the reason for bad memories. In our study more than 79% of the endometriosis patients answered that they have strong complaints during menstruation. Of these patients, 42% had to deal with these complains from the beginning of their menstruation, which could be the reason for the unpleasant memories. However surprisingly, no correlation between the existence of complaints during menstruation and unpleasant memories of patients' first menstruation was found. The reason could be that the complaints couldn't be defined quantitatively, as no pain or complain scale was included in the questionnaire. This makes it impossible to evaluate the importance of the complaints.

It is interesting that in our study there was a positive correlation between a negative memory of the first menstrual period and the aggravation of chronic pain associated with endometriosis. Patients with a negative memory of their first period claim a higher VAS score over the previous four weeks at the time of filling out the questionnaire. In addition, 30% of the pain group had negative memories of their mother concerning their menstruation, in comparison to 8% of the pain-free group. It is also interesting that there we found a correlation (P = 0.2) between a negative reaction of their mother concerning their menstruation and the aggravation of pain. Patients whose mothers had a negative reaction to their first period gave higher VAS score in the last 4 weeks (VAS=5.2) in comparison to

people of pain and a positive memory of their menstruation (VAS=4.6, N=23). We assume that women who suffered from rejection from their family over their period and their physiological body changes during adolescence may be more sensitive to pain.

Sexual and physical abuse

While multiple psychological factors have been linked to CPP, the role of sexual abuse in the development of CPP has been a subject of particular interest. Sexual abuse, physical abuse, or some other type of problematic relationship with the family during childhood or adolescence has been correlated with chronic pain in adults [2, 14, 20]. A history of sexual abuse is considered to be an important element of pain perception: modifying pain experiences and the ability to cope with pain [54, 55]. However, the results from the existing, limited-in-number studies up to now have been contradictory. Most studies showed that abuse, both in childhood and adult life is higher among women with CPP than among pain-free women [35, 59], in contrast Fry and colleagues [61] found the incidence of sexual abuse in their sample to be similar to that of the general population. However, they pointed out that sexual abuse might still be related to the development of CPP in some subgroups of patients. Toomey et al [64] made an attempt to explain the possible effects of abuse on pain variables in CPP patients. In their study, women who had experienced abuse in childhood reported greater punishing responses to pain and higher levels of somatization. They hypothesized that the punishing reports may suggest that the pain itself becomes a focus of perceived abuse, which continues to the present.

In our study there was no difference regarding life events in childhood between the control group and pain group. Pearce [24] suggested that events in childhood other than sexual abuse might play a role in the development of pelvic pain. The author found that a group of women with CPP without obvious pathology presented greater exposure to death and illness in family members and friends, in comparison to the CPP group with identifiable pathology. In our study no general difference with regard to such events during childhood between the endometriosis and the control group or between the sub-pain groups was found.

However, by examining more specific aspects of participants' childhood we did find a correlation - indicating that people with pain did have a higher incidence of physical abuse. We found that the pain group was more physically and emotionally abused during their childhood in comparison to the pain-free group: 45% of the pain group felt emotionally abused during their childhood in comparison to 22% of the control group. 19% of the patients

with pain believe they had been physically abused in comparison to 11% among the healthy population. More specifically, 18% of patients with pain in comparison to 8% of the control group answered that they did have bruises from physical abuse and 25% the patients with chronic pain answered that they had been beaten with heavy objects during their childhood in comparison to 11% of control group. These results support the hypothesis from Toomey [64] presented above.

No correlation with pain was present in either group regarding sexual abuse and inappropriate touching during childhood or adolescence. Rapkin et al. [65] found in their study no correlation between CPP and sexual abuse, although more women with CPP had experienced physical abuse than the pain free group. The investigators interpreted these findings as a negation of the unique relationship between sexual abuse and pelvic pain. They took these as a suggestion that abusive experiences, whatever their nature, may promote the chronicity of painful conditions.

The participants in our study tended to deny difficulties during childhood, but as the answers became more specific they gave more differentiated answers. This might be because of difficulty recalling such incidences without specification. We shouldn't also ignore the fact that these results are self-reported and the average time since childhood and adolescence was several years ago. Therefore, recall bias cannot be excluded.

Psychosomatic therapeutic options

Current therapies for the management of endometriosis and endometriosis-related symptoms concentrate on somatic aspects of the disease, targeting only its organic causes. A diversion from a pure "gynecological"- somatic approach of pain management, to psychosomatic management can be very beneficial among the endometriosis patients, especially when the currently available options for pain management do not give satisfying results (see above). Although surgery to remove endometriosis is effective in relieving pain in some women, symptom recurrence is common, and repeated medical and surgical interventions are often needed [18, 19]. About 20% of women show recurrent disease symptoms, especially pelvic pain, within 12 months after treatment [11]. However as pain symptoms in endometriosis patients do not necessarily correlate with the extent of the disease, another operation usually does not relieve symptoms. Also, there is little evidence regarding the risk factors for the recurrence of endometriosis, with regard to preoperative and postoperative pain. Renner et al [66] suggested that the risk for recurrence after surgery for endometriosis might be

substantially influenced by the patients' perception of pain. Risk classifications for the recurrence risk in endometriosis are non-existent. Developing these is imperatively needed to improve further treatment and prophylaxis for patients after surgery.

The relationship between endometriosis-associated pain and the factors reviewed in our project are very complex, as chronic pain can impact a person in many ways. Nevertheless we believe that psychosomatic management in endometriosis can help the patient understand her condition better, and develop new strategies to deal with the symptoms.
Patients' beliefs, attitudes and expectations of pain and its treatment should be included in the decision of the treatment approach. For other chronic populations, a consideration of patients' beliefs about the pain and ways of coping with it has been shown to affect perceptions of what people can do to relieve the pain [2]. The inclusion of chronic pain patients' perspectives in their treatment strategies has been found to affect pain perception, intensity and distress [2]. Information from the doctors on causes of the disease is essential for the feeling of control [11]. A sympathetic doctor who listens and takes womens' complains seriously, providing relevant information on therapeutic possibilities helps patients to develop their own ways coping with the disease, and builds trust in the patient-physician relationship.

Self-help organizations where affected women and their family can exchange experiences about the disease can be very helpful. Women who suffer from endometriosis very often feel socially isolated; as they experience that some people are unable to understand how endometriosis influences their everyday lives. In these groups, the affected women have the opportunity to be listened to and believed by others who share the same experiences. This helps build skills necessary to deal with the disease.

Coping strategies, relaxation techniques, and the avoidance of dysfunctional behaviors can help break the cycle of pain and increased body tension. This will help to reduce pain intensity [11]. Cognitive Behavioral Therapy (CBT) for pain can help endometriosis patients with pain to encourage helpful thought patterns, targeting a behavioral activation of healthy activities such as regular exercise and pacing. For example recent studies showed that CBT is more effective than standard care in treatment people with fibromyalgia [67, 68].

Systemic psychotherapy, hypnotherapy, acupuncture are some of the psychosomatic therapeutic options for pain management that should be also considered.

Strengths and weaknesses of the study

An advantage of the sample of pain group in our study was its homogeneity regarding the intensity and duration of pain. Also, the endometriosis group and the control group were very homogeneous regarding the age, civil status and monthly income. Another strength of the study was that the endometriosis group was one of the largest investigated groups regarding psychosomatic and psychosocial factors in the genesis of endometriosis-associated pain and the perception of pain. Furthermore, to our knowledge this is the first study, which compares systematically psychosocial aspects of endometriosis-related pain in endometriosis patients with healthy female population.

In the literature on chronic pain, investigators have examined several personality variables and certain patterns on personality inventories investigating their roles as predictors of pain [25, 26, 27]. However, the results of these studies have been contradictory, seeming to depend on the pain population sample. These findings point out the danger in generalizing from one chronic pain population to another, and the need to focusing on specific pain populations in order to lead to more accurate conclusions – the very task we have undertake here, investigating women with endometriosis and pain.

Furthermore, the current literature on the psychosomatic aspects of patients suffering from chronic painful diseases presents results from generally small study groups, or possesses methodological deficits. In order to investigate whether patients with endometriosis associated chronic pain share specific personal characteristics in comparison to other pain populations, the selection of the pain population has to be fairly and carefully chosen. We must ensure that the psychological status of the participants is independent of the severity and duration of their pain. Previous studies do not take such differentiation under consideration, limiting the impact of their results. In our study pain population was carefully chosen based in the same characteristics of chronic pain.

A point of criticism of our work is the fact that most endometriosis patients, 64%, are recruited from self-support centers, and so it cannot be excluded that the women from this group experience a greater impact of the disease in comparison to women with endometriosis from general population. However, it is especially from such high risk groups that we can learn about factors influencing pain and techniques to cope with the pain.

Another weakness of the study is the relative limited number of endometriosis patients. To better investigate the connection between characteristics of endometriosis and characteristics of pain more questionnaire participants are required. For example, it was difficult to arrive at conclusions about location of endometriosis lesions or types of lesions and characteristics of pain as only 31 of endometriosis patients answered to this question. Furthermore, as the endometriosis group included patients who had laparoscopies long before the start of our study, we can't be sure that the pain characteristics were not due to progress of the disease, current medication or therapies in between the operation and the time of our study.

The strategy of comparing endometriosis with the healthy population as well as with patients with chronic pain other origin could be very beneficial in understanding the complex factors involved in the perception and regulation of pain. Future studies will have to investigate larger population of endometriosis patients with more representative groups of women with such experiences.

7. Conclusions

Chronic pelvic pain in endometriosis patients is the most common symptom of endometriosis. The absence of a correlation between the endometriosis severity, and the presence of pain, suggests a possible link between psychosocial characteristics of the affected women and her perception and regulation of pain [34]. A few studies of psychological characteristics in women diagnosed with endometriosis have been published with contradictory results [9, 21, 22]. In our study we systematically investigated the psychological factors typically examined in the development of endometriosis but applied to the progression and perception of CPP in endometriosis patients.

We found that endometriosis patients who suffer from chronic pain have a higher prevalence of depression as well as anxiety. Our results show that they have been hospitalized in psychiatric institutions more often than women from the general population, or women with chronic pain other origin than endometriosis. Our investigation finds that people with a neurotic personality and mental disorders seem to develop chronic pain and disability more often. This agrees with previous studies [54, 55]. We found that a difficult acceptance of patient's menarche and the associated physiological body changes through adolescence is associated with the aggravation of chronic pain associated with endometriosis. A higher prevalence of physical and emotional abuse, both in childhood and in adult life was correlated with the presence and experience of pain.

In this study we investigated the psychosomatic factors that are most often related to endometriosis and chronic pain. According to the present results, various psychosomatic factors are involved in the perception and regulation of endometriosis-associated chronic pain. As pain continues to be an unsolved problem despite recent advances in medical science, the integration of certain psychological patterns into classical medical care could be beneficial. A greater awareness of the multifactorial causes of pain in endometriosis from physicians could be a potential option for the treatment of endometriosis-associated pain and beneficial for the women concerned.

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